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(54) PHAGE DISPLAYING SYSTEM EXPRESSING SINGLE CHAIN ANTIBODY

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U.S.C. 154(b) by 367 days.

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(22) Filed: May 20, 2013

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- (62) Division of application No. 12/854,632, filed on Aug. 11, 2010, now abandoned.
- (60) Provisional application No. 61/232,819, filed on Aug. 11, 2009.
- (51) Int. Cl.

 C40B 40/08 (2006.01)

 C12N 15/73 (2006.01)

 C07K 16/00 (2006.01)

 C07K 16/10 (2006.01)

 C07K 16/22 (2006.01)

 C12N 15/10 (2006.01)

 C40B 50/06 (2006.01)

(52) U.S. Cl.

(58) Field of Classification Search

None

See application file for complete search history.

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Prust et al. (Feb. 2005) Nature Biotechnology vol. 23 pp. 195 to 200.* Jestin et al.; (Feb. 2001) Research in Microbiology; 152:187-191. Rajagopal et al., "A form of anti-Tac(Fv) which is both single-chain and disulfide stabilized: comparison with its single-chain and disulfide-stabilized homologs", *Protein Engineering* vol. 10 No. 12 pp. 1453-1459, 1997.

(Continued)

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(57) ABSTRACT

Disclosed are nucleic acid libraries for identifying a signal peptide that facilitates production of disulfide-stabilized single chain antibody, and for facilitating production of a disulfide-stabilized single chain antibody. Also disclosed are host cell libraries and phage libraries including the nucleic acid libraries. Further disclosed are methods for identifying a signal peptide that facilitates production of disulfide-stabilized single chain antibody, and methods for producing a disulfide-stabilized single chain antibody and non-fusion form thereof.

16 Claims, 7 Drawing Sheets

Open reading frame starting site	
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Q ID NO:602 ATGACCATGATTACGCCAAGCTTTGGAGCCTTTTTTTTTGGAGATTTTCAACGTGA	
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QID NO:605L3 library CAACGTG/	LAAAAA
DID NO:606L4 library	AAAA
pelB peptidas€	
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-HHHHGHGSGDIQM-	
CATCAC	
CATCACCACCATCATGCCAC	
NNKNNKCACCATCATGGCCACGGGTCCG	

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Steiner et al., "Signal sequences directing cotranslational translocation expand the range of proteins amenable to phage display", *Nature Biotechnology* vol. 24 No. 7 pp. 823-831, 2006. Young et al., "Thermal stabilization of a single-chain Fv antibody fragment by introduction of a disulphide bond", *FEBS Letters* 377

(1995) 135-139.

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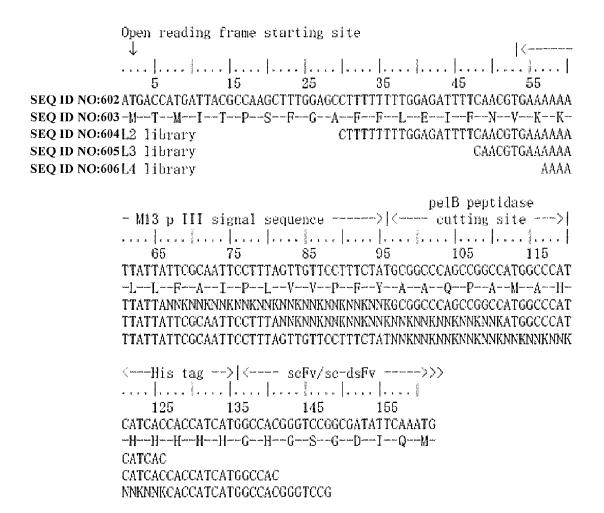
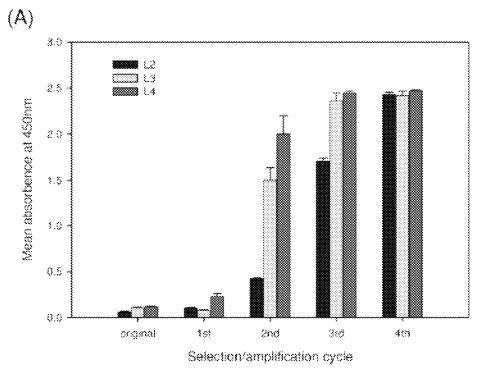


FIG. 1



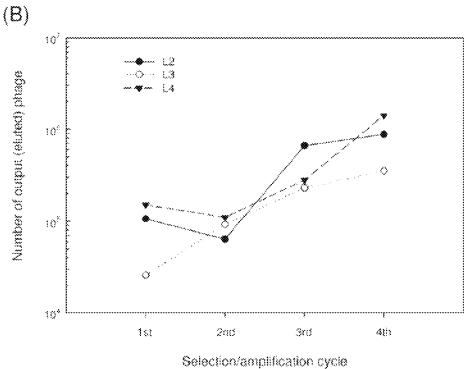


FIG. 2

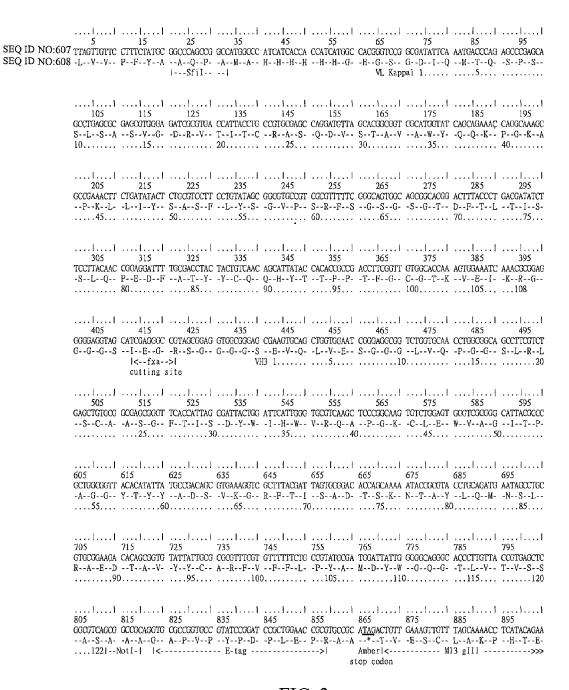


FIG. 3

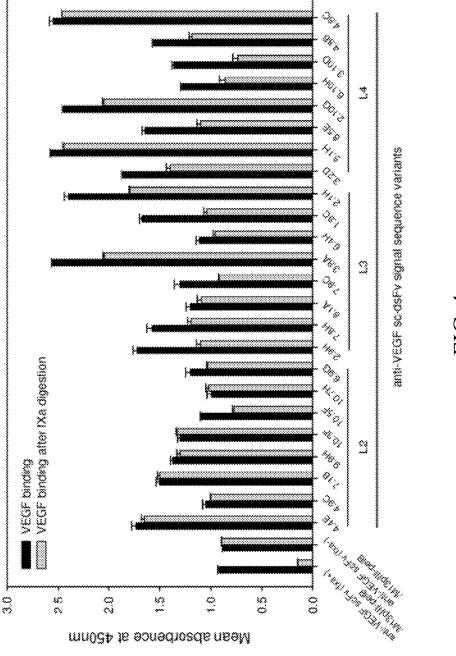


FIG. 4

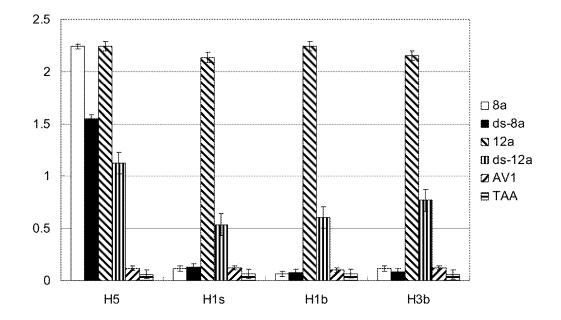


FIG. 5

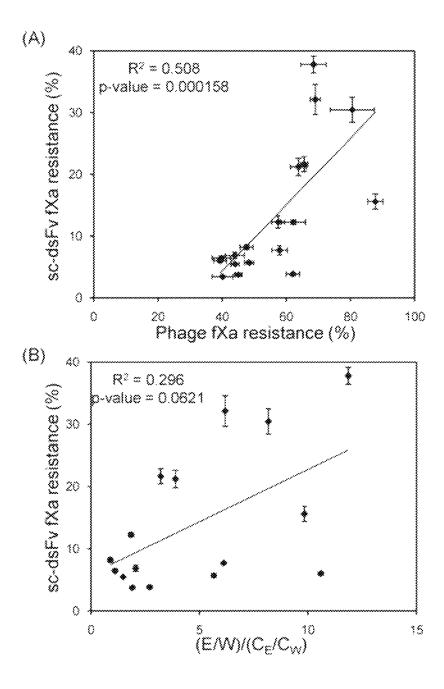


FIG. 6

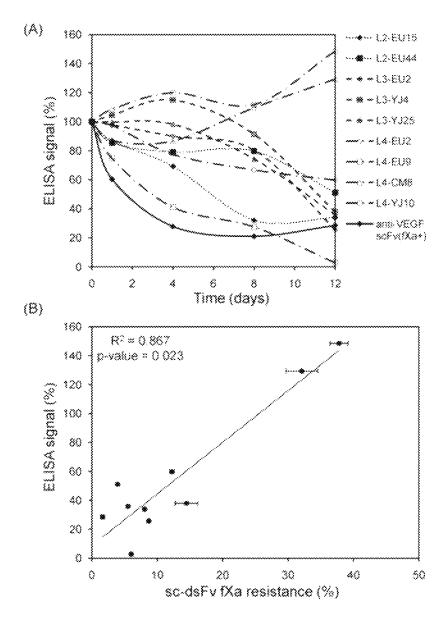


FIG. 7

PHAGE DISPLAYING SYSTEM EXPRESSING SINGLE CHAIN ANTIBODY

RELATED APPLICATIONS

This application is a divisional of U.S. application Ser. No. 12/854,632, filed on Aug. 11, 2010, which claims priority to U.S. Provisional Application No. 61/232,819, filed on Aug. 11, 2009. The contents of both prior applications are incorporated by reference in their entirety.

FIELD OF THE INVENTION

The present invention is related to a phage displaying system expressing disulfide-stabilized single chain antibody variable fragments (sc-dsFv).

BACKGROUND OF THE INVENTION

A single chain variable fragment (scFv) is a single polypeptide chain antibody fragment having a light chain variable domain and a heavy chain variable domain, with a flexible linkage peptide connecting the two domains. An scFv displayed as a fusion protein N-terminal to the pIII minor capsid protein on filamentous phage surface is one of the most prominent methods in antibody engineering. It was reported that the small size of the scFv enabled superior tissue-penetrating capabilities over whole IgG or Fab fragment, making scFv an ideal scaffold for designing tumor-homing molecules carrying therapeutic or imaging agents (Michnick, S. W., and Sidhu, S. S. (2008) *Nat Chem Biol* 4(6), 326-329).

Yet, under practical application conditions, an scFv scaffold tends to form aggregation. The aggregation has much to do with the stability of the two variable domains and the 35 dimeric interface. The instability of the scFv structure also compromises the fidelity in reproducing the antibody gene products on phage surface, causing biases in favor of more stable scFv molecules over the less stable ones, or selecting non-folded structures on phage surfaces but nevertheless 40 binding to an antigen. This structural instability thus impacts negatively on the applications of scFv in biotechnology and medical uses.

One way to stabilize the scFv scaffold is to engineer a disulfide bond between the two Fv domains, so that the variable domains can be covalently linked with a disulfide bond. Single chain disulfide-stabilized Fv fragment (sc-dsFv) format was constructed in a single polypeptide chain, as in scFv, with a disulfide framework region (Young, N. M. et al., (1995) *FEBS Lett* 377(2), 135-139; Worn, A., and Pluckthun, A. (1999) *Biochemistry* 38(27), 8739-8750). The sc-dsFv molecules could be expressed in *E. coli*, but not be expressed on phage surface or as soluble form secreted by *E. coli* in a culture medium, mostly due to severely decreased yield because of the introduction of interface cysteines (Worn, A., and Pluckthun, A. (2001) J Mol Biol 305(5), 989-1010).

Up to now, phage-displayed sc-dsFv libraries and their applications have not been established.

BRIEF SUMMARY OF THE INVENTION

The invention provides a methodology to systematically optimize the signal sequences for phage-displayed protein expression, for which the expression with conventional signal sequences was not viable. The optimized signal sequences and related discovering methodologies led to the establishment of phage display systems with the sc-dsFv format,

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enabling the demonstration and comparison of the performance of the sc-dsFv phage display platform with that of the conventional scFv platform.

Accordingly, in one aspect, the present invention provides a nucleic acid library for identifying a signal peptide that facilitates production of disulfide-stabilized single chain antibody. The library includes a plurality of expression constructs, each of which includes: a first nucleotide sequence encoding a signal peptide, and a second nucleotide sequence encoding a single chain antibody capable of forming an interface disulfide bond. The second nucleotide sequence is located 3' downstream to the first nucleotide. The signal peptide has the amino acid sequence of:

- 15 (a) VKKLLX $_1$ X $_2$ X $_3$ X $_4$ X $_5$ X $_6$ X $_7$ X $_8$ X $_9$ X $_{10}$ AAQPAMA HHH-HHHGH (SEQ ID NO:1),
 - (b) VKKLLFAIPLX₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀MAHH HHHHGH (SEQ ID NO:2), or
- 20 (c) VKKLLFAIPLVVPFYX $_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}$ HHHGH (SEQ ID NO:3).

each of X_1 - X_{10} in (a), (b), and (c) is one of the 20 naturally occurring amino acid residues.

In another aspect, the invention provides a host cell library for identifying a signal peptide that facilitates production of disulfide-stabilized single chain antibody. The library includes a plurality of host cells each containing an expression construct that includes: a first nucleotide sequence encoding a signal peptide, and a second nucleotide sequence encoding a single chain antibody capable of forming an interface disulfide bond; the second nucleotide sequence is located 3' downstream to the first nucleotide; the signal peptide has the amino acid sequence of

- (a) VKKLLX $_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}$ AAQPAMAH HHHHHGH (SEQ ID NO:1),
- (b) VKKLLFAIPLX $_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}$ MAHH HHHHGH (SEQ ID NO:2), or
- (c) VKKLLFAIPLVVPFYX $_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}$ HHHGH (SEQ ID NO:3).

each of X_1 - X_{10} in (a), (b), and (c) is one of the 20 naturally occurring amino acid residues.

In another aspect, the invention provides a phage library for identifying a signal peptide that facilitates production of disulfide-stabilized single chain antibody. The library has a plurality of phage particles each containing a disulfide-stabilized single chain antibody fused with a coat protein on the surface of the phage. The phage library is prepared by the steps of: providing a host cell containing an expression construct, and culturing the host cell in a medium under conditions allowing expression of the plurality of phage particles; the expression construct that includes a first nucleotide sequence encoding a signal peptide, a second nucleotide sequence encoding a single chain antibody capable of faulting an interface disulfide bond, the second nucleotide sequence being located 3' downstream to the first nucleotide, and a third nucleotide sequence encoding a phage envelop protein; the third nucleotide sequence being located 3' downstream to the second nucleotide sequence; the signal peptide has the amino acid sequence of

- (a) VKKLL $X_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}$ AAQPAMA HHH-HHHGH (SEQ ID NO:1),
- (b) VKKLLFAIPLX₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀MAHHH HHHGH (SEQ ID NO:2), or
- (c) VKKLLFAIPLVVPFYX $_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}$ H 5 HHGH (SEQ ID NO:3),

each of X_1 - X_{10} in (a), (b), and (c) being one of the 20 naturally occurring amino acid residues.

In addition, the invention provides a sc-dsFv phage display platform. According to the invention, a large scale screening 10 for optimal signal sequences was carried out. In one example of the invention, the signal sequences that were effective for phage-displayed sc-dsFv and non-fusion soluble sc-dsFv secretion in *E. coli* Amber suppressor strain ER2738 were screened to obtain the sequence preference patterns emerged 15 from the optimum signal sequences.

In still another aspect, the present invention provides an isolated nucleic acid, having a first nucleotide sequence encoding a signal peptide, and a second nucleotide sequence encoding a single chain antibody capable of forming an interface disulfide bond. The signal peptide has the amino acid sequence of

(a) VKKLLX₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀AAQPAMAHHH HHHGH (SEQ ID NO: 596), in which X₁ is A, C, F, G, I, L, M, 25 P, Q, S, V, W, or Y; X₂ is A, D, F, G, H, I, L, M, N, P, S, T, V, or W; X₃ is A, F, G, L, M, P, Q, R, S, T, V, or W; X₄ is A, F, G, H, I, L, M, P, Q, R, S, T, V, W, or Y; X₅ is A, C, D, F, G, H, I, L, M, P, Q, R, S, T, V, W, or Y; X₆ is A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X₇ is A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X₈ is A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X₉ is A, C, D, E, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; and X₁₀ is A, C, D, E, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; and X₁₀ is A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y;

 $\begin{array}{l} \text{VKKLLFAIPLX}_{1}X_{2}X_{3}X_{4}X_{5}X_{6}X_{7}X_{8}X_{9}X_{10}\text{MAHHHH} \\ \text{HHGH (SEQ ID NO:597), in which } X_{1}\text{ A, C, F, G, H, I, L, M, N, P, Q, S, T, V, W, or Y; } X_{2}\text{ is A, C, D, F, G, H, I, L, M, P, Q, R, S, T, V, W, or Y; } X_{3}\text{ is A, C, D, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; } X_{4}\text{ is A, C, E, F, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; } X_{5}\text{ is A, C, D, F, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; } X_{6}\text{ is A, C, D, E, F, G, H, K, L, M, P, Q, R, S, T, V, W, or Y; } X_{7}\text{ is A, D, E, F, G, H, K, L, M, N, P, Q, R, S, T, V, or Y; } X_{8}\text{ is A, C, F, G, I, K, L, M, N, P, Q, R, S, T, V, or Y; } X_{8}\text{ is A, C, F, G, I, K, L, M, N, P, Q, R, S, T, or V, } X_{9}\text{ is A, C, D, F, H, L, M, N, P, Q, R, S, T, V, W, or Y; } \text{and } X_{10}\text{ is A, C, D, } 45\text{ E, F, G, H, L, M, P, Q, R, S, or T; or} \end{array}$

 $\begin{array}{l} VKKLLFAIPLVVPFYX_{1}X_{2}X_{3}X_{4}X_{5}X_{6}X_{7}X_{8}X_{9}X_{10}HH\\ HGH (SEQ ID NO:598), in which X_{1} is A, C, D, F, G, I, L, M,\\ N, P, Q, R, S, T, V, or Y; X_{2} is A, C, D, F, G, H, K, L, N, P, Q,\\ R, S, T, V, W, or Y; X_{3} is A, C, E, F, G, H, I, K, L, M, N, P, Q,\\ R, S, T, V, W, or Y; X_{4} is A, C, D, F, G, H, I, L, M, N, P, Q, R,\\ S, T, V, W, or Y; X_{5} is A, C, E, F, G, H, I, K, L, M, N, P, Q, R,\\ S, T, W, or Y; X_{5} is A, C, E, F, G, H, I, K, L, M, N, P, Q, R,\\ S, T, V, W, or Y; X_{7} is A, D, E, F, G, H, I, K, L, M, N, P, Q, R,\\ S, T, V, or Y; X_{8} is A, E, F, G, H, I, K, L, M, N, P, Q, R, S, T,\\ V, W, or Y; X_{9} is A, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V,\\ W, or Y; and X_{10} is A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, or Y. \end{array}$

In a further aspect, the present invention provides a host 60 cell containing the nucleic acid described above.

In a further more aspect, the present invention provides a phage containing a disulfide-stabilized single chain antibody fused with its coat protein on the surface. The phage is prepared by a method having the steps of: providing the above-described host cell, and culturing the host cell in a medium under conditions allowing expression of the phage.

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In further another aspect, the present invention provides a method for producing a disulfide-stabilized single chain antibody. The method includes the steps of providing a host cell containing an expression construct, and culturing the host cell in a medium under conditions allowing expression of the disulfide-stabilized single chain antibody. The expression construct includes a first nucleotide sequence encoding a signal peptide, and a second nucleotide sequence encoding a single chain antibody capable of forming an interface disulfide bond; the signal peptide has the amino acid sequence of:

 $\begin{array}{l} \text{VKKLLX}_{1}X_{2}X_{3}X_{4}X_{5}X_{6}X_{7}X_{8}X_{9}X_{10}\text{AAQPAMAHHH} \\ \text{HHHGH (SEQ ID NO: 596), in which X_{1} is $A, C, F, G, I, L, M, P, Q, S, V, W, or $Y; X_{2}$ is $A, D, F, G, H, I, L, M, N, P, S, T, V, or $W; X_{3}$ is $A, F, G, L, M, P, Q, R, S, T, V, or $W; X_{4}$ is $A, F, G, H, I, L, M, P, Q, R, S, T, V, W, or $Y; X_{5}$ is $A, C, D, F, G, H, I, L, M, P, Q, R, S, T, V, W, or $Y; X_{6}$ is $A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or $Y; X_{7}$ is $A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or $Y; X_{8}$ is $A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or $Y; X_{9}$ is $A, C, D, E, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or $Y; and X_{10} is $A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or $Y; (b) \end{array}$

VKKLLFAIPLX₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀MAHHHH HHGH (SEQ ID NO: 597), in which X₁ A, C, F, G, H, I, L, M, N, P, Q, S, T, V, W, or Y; X₂ is A, C, D, F, G, H, I, L, M, P, Q, R, S, T, V, W, or Y; X₃ is A, C, D, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; X₄ is A, C, E, F, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X₅ is A, C, D, F, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; X₆ is A, C, D, E, F, G, H, K, L, M, P, Q, R, S, T, V, W, or Y; X₇ is A, D, E, F, G, H, K, L, M, N, P, Q, R, S, T, V, or Y; X₈ is A, C, F, G, I, K, L, M, N, P, Q, R, S, T, or V, X₉ is A, C, D, F, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; H, I, L, M, N, P, Q, R, S, T, V, W, or Y; and X₁₀ is A, C,
 D, E, F, G, H, L, M, P, Q, R, S, or T; or

(c) VKKLLFAIPLVVPFYX $_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}H$ HHGH (SEQ ID NO:598), in which X_1 is A, C, D, F, G, I, L, M, N, P, Q, R, S, T, V, or Y; X_2 is A, C, D, F, G, H, K, L, N, P, Q, R, S, T, V, W, or Y; X_3 is A, C, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X_4 is A, C, D, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; X_5 is A, C, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, W, or Y; X_5 is A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X_7 is A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, or Y; X_8 is A, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X_9 is A, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; and X_{10} is A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, or Y.

In addition, the present invention provides a new signal peptide that facilitates production of disulfide-stabilized single chain antibody, and the nucleic acid encoding the signal peptide.

The details of one or more embodiments of the invention are set forth in the description below. Other features, objects, and advantages of the invention will be apparent from the description and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing summary, as well as the following detailed description of the invention, will be better understood when read in conjunction with the appended drawings. It should be understood, however, that the invention is not limited to the precise arrangements and instrumentalities shown.

FIG. 1 is a schema showing the signal sequence in pCANTAB5E and the constructs of DNA libraries to diversify the tentative signal sequence responsible for the expression of the phage-displayed pIII fusion proteins.

FIG. 2 is a set of diagrams showing the results of the increased binding to VEGF for phage-displayed sc-dsFv signal sequence variants enriched from the three libraries after selection/amplification cycles, including (A) after each round of selection/amplification cycle, the values of the binding of 5 the rescued phage to immobilized VEGF as measured with ELISA. The ELISA signal strengths are shown in the y-axis, as functions of the selection/amplification cycle; and (B) the numbers of output phage particles titered after each round of selection/amplification cycle for each of the three libraries; 10 the output phage titers, as shown in the y-axis, were plotted against the number of the selection/amplification cycles.

FIG. 3 is a schema showing the DNA construct of the S5 anti-VEGF sc-dsFv as a pIII fusion protein in the pCANTAB5E phagemid.

FIG. 4 is a diagram showing VEGF-binding strengths of the phage-displayed anti-VEGF sc-dsFv's from various signal sequence variants with or without fXa digestion. Eight variants with maximal fXa digestion resistance from a 96-well ELISA plate containing 96 randomly picked variants 20 were selected from each of the VEGF-binding enriched libraries after the 4th round of selection/amplification cycle. These variants were cultured and the rescued phages were allowed to bind to immobilized VEGF with (grey histogram) and without (black histogram) the fXa treatment, and the 25 VEGF-binding strengths (y-axis) were measured with ELISA. The error bars were derived from three repeats of the ELISA measurement.

FIG. 5 is a diagram showing the binding strengths of phage-displayed anti-HAs scFv/sc-dsFv. One of the scFv 30 phages with specific binding ability to H5, 8a, and the other one with broad-spectrum ability to HAs, 12a, were engineered to disulfide-stabilized scFv (ds-scFv) formats; the scdsFv construct was different from the scFv construct in the mutations (L:Gly100Cys & H:Gly44Cys). Av1 was negative 35 control of an scFv displayed on the phage; and TAA means the phage does not contain any displayed protein; and various HA subtypes were precoated to ELISA wells to determined binding activity, and the error bars were derived from three repeats of the ELISA measurements.

FIGS. 6A and B are diagrams showing correlations between sc-dsFv folding quality and resistance to fXa digestion. FIG. 6A shows a comparison of the extents (percentages) of the interface disulfide bond formation of the sc-dsFv from the optimum signal sequence variants from L4; both of 45 the axes show the ratio (percent) of the ELISA signal for VEGF-binding after the fXa treatment over the ELISA signal for VEGF-binding before the fXa treatment; the y-axis shows the data from secreted sc-dsFv; the x-axis shows the data from phage-displayed sc-dsFv. FIG. 6B shows a comparison of the 50 could not be expressed on phage surface, and why the disulextents (percentages) of the interface disulfide bond formation (y-axis) with the folding quality (x-axis) of the sc-dsFv from the optimum signal sequence variants from L4. The sc-dsFv folding quality (x-axis) is represented as the sc-dsFv-VEGF binding ELISA signal divided by western blot signal 55 probed with anti-E tag antibody (E/W, VEGF binding signal divided by secreted sc-dsFv quantity), and then the ratio is normalized with that of anti VEGF scFv (fXa+) (CE/CW, VEGF binding signal divided by secreted scFv quantity), that is, the folding quality is quantified with the ratio: (E/W)/(CE/ 60 CW); the error bars in each data point indicate the standard deviations from three repeats of the experiment; the coefficient of determination R2 and the p-value from Spearman's rank correlation coefficient was shown in each panel.

FIGS. 7A and B are diagrams showing stability test of 65 soluble sc-dsFv; including FIG. 7A showing the results of the soluble sc-dsFv incubated at 37° C. as the indicated time

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shown in the x-axis, and the binding capacities estimated with ELISA against VEGF, shown in y-axis; the ELISA signal was normalized against that of the secreted protein kept at 4° C.; and FIG. 7B showing the fXa resistance percentages of the soluble sc-dsFv plotted against the end binding capacities after 12 days of incubation in 37° C.; the error bars in each data point indicate the standard deviations from three repeats of the experiment, and the coefficient of determination R2 and the p-value from Spearman's rank correlation coefficient are shown in the panel.

DETAILED DESCRIPTION OF THE INVENTION

Unless defined otherwise, all technical and scientific terms used herein have the meaning commonly understood by a person skilled in the art to which this invention belongs. As used herein, the following terms have the meanings ascribed to them unless specified otherwise.

The articles "a" and "an" are used herein to refer to one or more than one (i.e., at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

Amino acids can be expressed by three letters or one letters. Table 1 lists standard amino acid abbreviations.

TABLE 1

Standard amino acid abbreviations						
Amino Acid	3-Letter	1-Letter				
Alanine	Ala	A				
Arginine	Arg	R				
Asparagine	Asn	N				
Aspartic acid	Asp	D				
Cysteine	Cys	C				
Glutamic acid	Glu	E				
Glutamine	Gln	Q				
Glycine	Gly	G				
Histidine	His	H				
Isoleucine	Ile	I				
Leucine	Leu	L				
Lysine	Lys	K				
Methionine	Met	M				
Phenylalanine	Phe	F				
Proline	Pro	P				
Serine	Ser	S				
Threonine	Thr	T				
Tryptophan	Trp	W				
Tyrosine	Tyr	Y				
Valine	Val	V				

Very little is known as to why some sc-dsFv constructs fide bonds of the newly synthesized preprotein can only be formed in the oxidizing environment of periplasm. The mechanism for the translocation of the nascent unfolded polypeptide chain from the translation site in the cytoplasm across the periplasmic membrane could be a key determinant for the folding. It was unexpectedly found in the invention that for the expression of the displayed protein on the phage surface, alternative sequences in the signal peptide region can modulate the expression level and folding quality of the displayed protein. Accordingly, the invention provides a methodology to systematically optimize the signal sequences for phage-displayed protein expression. Based on the optimized signal sequences and the methodologies of the invention, phage display systems with the sc-dsFv format are established.

According to the present invention, a nucleic acid library for identifying a signal peptide that facilitates production of

disulfide-stabilized single chain antibody is provided. The library has a plurality of expression constructs, each of which includes: a first nucleotide sequence encoding a signal peptide, and a second nucleotide sequence encoding a single chain antibody capable of forming an interface disulfide 5 bond. The second nucleotide sequence is located 3' downstream to the first nucleotide. The signal peptide has the amino acid sequence of:

- (a) VKKLLX₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀AAQPAMAHH HHHHGH (SEQ ID NO: 1),
- (b) VKKLLFAIPLX $_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}$ MAHHH HHHGH (SEQ ID NO:2), or
- (c) VKKLLFAIPLVVPFYX₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀H HHGH (SEQ ID NO:3),

each of X_1 - X_{10} in (a), (b), and (c) being one of the 20 naturally 15 occurring amino acid residues.

In one embodiment, each of the expression constructs further includes a third nucleotide encoding a phage coat protein, and the third nucleotide sequence being located 3' downstream to the second nucleotide.

The term "signal peptide" or "signal sequence" used herein refers to a short (i.e. 3-60 amino acids long) peptide chain that directs the transport of a protein. The signal peptide is known to be responsible for the sec system-dependent translocation of the sc-dsFv-pIII fusion from the translation site in cyto- 25 plasm across the periplasmic membrane, a critical process for the integration of the displayed protein on the recombinant phage. Considering the vast signal peptide sequence space needed to be explored, the present invention provides biological combinatorial strategies to diversify the signal peptide 30 sequences with synthetic phage display libraries. The variants in the phage libraries were selected and screened for high expression capabilities, so as to identify the key regions of the signal peptide sequences, including the optimal amino acid sequences, positions and types that are effectively respon- 35 sible for the sc-dsFv expression on phage surface.

The term "single chain variable fragment" or "scFv" used herein refers to a single polypeptide chain antibody fragment construct encoding a first variable region and a second variable region, with a flexible linkage peptide connecting the two 40 domains. The first and the second variable region can be either a light chain or a heavy chain variable region. The recombinant antibody fragment frequently retains antigenrecognizing capability rivaling that of the parent antibody. One shortcoming of the scFv scaffold is the aggregation ten- 45 dency of the scFv molecules under physiological and storage conditions. The aggregation mechanism has much to do with the stability of the two variable domains and the dimeric interface. This structural instability has thus impacted negatively on the utilities of scFv, leading to uncertainties to the 50 outcomes of the selected and screened scFv molecules in terms of their potential applications in biomedicine.

The term "disulfide-stabilized single chain antibody variable fragment" or "sc-dsFv" used herein refers to a single polypeptide chain containing two variable regions capable of 55 forming an interface disulfide bond, where each of the two variable regions may be a heavy chain variable region or a light chain variable region. According to the invention, the sc-dsFv-pIII fusion protein can be prepared by using the optimal signal sequences capable of directing the sc-dsFv 60 expression on phage surface.

In an embodiment of the invention, the overlapping segments encompassing the complete signal sequence region governing the protein trafficking of the model anti-VEGF sc-dsFv fusion protein were searched with biological combinatorial methodology for sequence preferences leading to effective expression of the sc-dsFv. The engineering platform

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established for the disulfide-stabilized antibody variable domain fragment as demonstrated could be used to prepare many of scFv molecules in a more stable structure, which could be carried out under harsh conditions, and have longer shelf-life.

According to one embodiment of the invention, to select signal sequences for effective expression of anti-VEGF scdsFv on M13 phage surface, phage display libraries L2, L3 and L4 were constructed to diversify the signal sequence as shown in FIG. 1, where M13PIII-pelB indicated the signal sequence being the wild type signal sequence for pIII in M13 phage genome in connection with pelB peptidase cleavage site. The complexities of the L2, L3 and L4 phage display library were 3.1×10°, 3.7×10°, and 1.5×10°, respectively. These libraries were designed to efficiently diversify the signal peptide sequences on identifying the optimum signal peptides for expression sc-dsFv.

In one example of the invention, the expression construct is a phagemid. Among the expression constructs, the nucleotide sequence of the signal peptide, sc-dsFv and the phage coat protein could be operatively linked in a random order. In one preferred example of the invention, the second nucleotide sequence encoding sc-dsFv is located 3' downstream to the 25 first nucleotide encoding the signal peptide, and the third nucleotide sequence encoding the phage coat protein is located 3' downstream to the second nucleotide sequence.

In one embodiment of the invention, a sc-dsFv library, containing more than one billion sc-dsFv variants, is propagated with an *E. coli* vector of bacterial phage origin following the method as described by McCafferty, J. et al. (*Nature* 348(6301), 552-554, 1990). The recombinant phages displaying the sc-dsFv variants can be selected or screened for antigen-binding and re-amplified with the host cells, i.e. *E. coli*

Furthermore, the present invention provides a host cell library for identifying a signal peptide that facilitates production of disulfide-stabilized single chain antibody. The library includes a plurality of host cells each containing the aforementioned expression constructs.

The present invention also provides a phage library for identifying a signal peptide that facilitates production of disulfide-stabilized single chain antibody. The library includes a plurality of phage particles each containing a disulfide-stabilized single chain antibody fused with a coat protein on the surface of said phage. The phage library is prepared by the steps of: providing a host cell containing an expression construct, and culturing the host cell in a medium under conditions allowing expression of the plurality of phage particles. The expression construct includes (1) a first nucleotide sequence encoding a signal peptide, (2) a second nucleotide sequence encoding a single chain antibody capable of forming an interface disulfide bond, the second nucleotide sequence being located 3' downstream to the first nucleotide, and (3) a third nucleotide sequence encoding a phage envelop protein, the third nucleotide sequence being located 3' downstream to the second nucleotide sequence. The signal peptide has the amino acid sequence of

- (a) VKKLL $X_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}$ AAQPAMAH HHHHHGH (SEQ ID NO:1),
- (b) VKKLLFAIPL $X_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}$ MAHHH HHHGH (SEQ ID NO:2), or

 $VKKLLFAIPLVVPFYX_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}H\\$ HHGH (SEQ ID NO:3),

each of X_1 - X_{10} in (a), (b), and (c) is one of the 20 naturally occurring amino acid residues.

On the other hand, a sc-dsFv engineering platform is established for preparation of scFv molecules in a more stable structure in the present invention. Accordingly, the present invention provides an isolated nucleic acid that has a first nucleotide sequence encoding a signal peptide, and a second nucleotide sequence encoding a single chain antibody 10 capable of forming an interface disulfide bond. The second nucleotide sequence is located 3' downstream to the first nucleotide. The signal peptide has the amino acid sequence of (a)

 $VKKLLX_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}AAQPAMAHHH\\$ HHHGH (SEQ ID NO: 596), in which X₁ is A, C, F, G, I, L, M, P, Q, S, V, W, or Y; X₂ is A, D, F, G, H, I, L, M, N, P, S, T, V, or W; X₃ is A, F, G, L, M, P, Q, R, S, T, V, or W; X₄ is A, F, G, H, I, L, M, P, Q, R, S, T, V, W, or Y; X₅ is A, C, D, F, G, H, I, L, M, P, Q, R, S, T, V, W, or Y; X₆ is A, C, D, F, G, H, I, K, L, 20 M, N, P, Q, R, S, T, V, W, or Y; X₇ is A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X₈ is A, C, D, E, F, G, H, I, K, $L,M,N,P,Q,R,S,T,V,W, or\,Y;X_9\,is\,A,C,D,E,F,G,H,I,\\$ L, M, N, P, Q, R, S, T, V, W, or Y; and X₁₀ is A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y;

(b) VKKLLFAIPLX₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀MAHHH HHHGH (SEQ ID NO:597), in which X₁ is A, C, F, G, H, I, L, M, N, P, Q, S, T, V, W, or Y; X₂ is A, C, D, F, G, H, I, L, M, P, Q, R, S, T, V, W, or Y; X₃ is A, C, D, F, G, H, I, L, M, N, P, Q, $R, S, T, V, W, \text{ or } Y; X_{\Delta} \text{ is } A, C, E, F, H, I, K, L, M, N, P, Q, R, 30$ S, T, V, W, or Y; X₅ is A, C, D, F, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; X₆ is A, C, D, E, F, G, H, K, L, M, P, Q, R, S, T, V, W, or Y; X₇ is A, D, E, F, G, H, K, L, M, N, P, Q, R, S, T, V, or $Y; X_8 \text{ is } A, C, F, G, I, K, L, M, N, P, Q, R, S, T, \text{ or } V; X_9 \text{ is } A,$ C, D, F, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; and X₁₀ is A, 35 C, D, E, F, G, H, L, M, P, Q, R, S, or T; or

(c) VKKLLFAIPLVVPFYX₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀H HHGH (SEQ ID NO:598), in which X₁ is A, C, D, F, G, I, L, M, N, P, Q, R, S, T, V, or Y; X₂ is A, C, D, F, G, H, K, L, N, P, Q, R, S, T, V, W, or Y; X₃ is A, C, E, F, G, H, I, K, L, M, N, P, 40 of disulfide-stabilized single chain antibody were obtained Q, R, S, T, V, W, or Y; X₄ is A, C, D, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; X₅ is A, C, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, W, or Y; X₆ is A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X₇ is A, D, E, F, G, H, I, K, L, M, N, P, Q, $R,\,S,\,T,\,V,\,or\,Y;\,X_{8}\,\,is\,A,\,E,\,F,\,G,\,H,\,I,\,K,\,L,\,M,\,N,\,P,\,Q,\,R,\,S,\,\,\,45$ T, V, W, or Y; X₉ is A, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, $V, W, \text{ or } Y; \text{ and } X_{10} \text{ is } A, D, E, F, G, H, I, K, L, M, N, P, Q, R,$ S, T, V, or Y.

According to the invention, the nucleic acid further includes a third nucleotide encoding a phage coat protein. The 50 third nucleotide sequence is located 3' downstream to the second nucleotide sequence.

In one example of the invention, anti-VEGF sc-dsFv phage display platform was developed. As shown in FIG. 1, expression constructs for identifying a signal peptide that facilitates 55 production of disulfide-stabilized single chain antibody were designed. Each of the three DNA libraries (L2, L3, and L4) contained ten consecutive NNK degenerate codons covering overlapping regions around the signal sequence. N stands for A, G, T, or C, 25% each; K stands for G or T, 50% each. The 60 NNK degenerated codon represents 32 possible triplet combinations, encoding all 20 natural amino acids and an amber stop codon (TAG). Each of the phage display libraries was selected for binding against immobilized VEGF. The trends of enrichment of the VEGF-binding phage variants from each of the three libraries, plotted as functions of the number of selection/amplification cycle, are shown in FIG. 2. The

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enrichment trends were similar among the variants from the three libraries. This result indicates that the signal sequence regions covered by the three signal sequence libraries (see FIG. 1) can all be optimized to increase the expression of the correctly folded anti-VEGF sc-dsFv on phage surface.

In order to further identify binding variants, more than 3000 colonies were randomly selected from each of the libraries L2, L3, and L4 after selection/amplification cycles for enrichment of the binding variants. These phage colonies were individually rescued and spotted on nitrocellulose membranes coated with VEGF (100 µg/30 ml). According to the invention, each of the signal peptides having the amino acid sequences of SEQ ID NOS: 5-593 as listed in Tables 2, 3 and 4 was obtained and proved to be capable of facilitating the expression of the sc-dsFv on phage surface. After normalization based on the standard phage solution signals in each of the blocks, the phage-displayed scFv expression efficiency for each of the samples was calculated with the following equation:

Ratio =
$$\frac{\text{sample}(CV)}{\text{sample}(C0)} / \frac{\text{control}(CV)}{\text{control}(C0)}$$

The value of the sample (CV) is the average normalized signal from VEGF-coated membrane; that of the sample (C0) is the averaged normalized signal from the un-coated and un-blocked membrane. Similarly, those of the control (CV) and control (C0) are the averaged normalized signals for the control phage in the same block where the sample signals are measured on corresponding membrane. The ratio derived from the equation was used to rank the efficiency of the sample phage binding to the immobilized VEGF. All the phage samples with measurable binding strengths with the immobilized VEGF were ranked; the signal sequences of the top fifty ranked phage samples are shown and marked with "*" in Tables 2-4.

Accordingly, new signal peptides that facilitate production (see Example 2). In the embodiment of the invention, the signal peptide selected from the group consisting of the peptides having the amino acid sequences set forth in SEQ ID NOS: 5-593 were proved to facilitate production of disulfidestabilized single chain antibody. On the other hand, a new isolated nucleic acid encoding the above mentioned signal peptide was provided as well.

In a preferred embodiment of the invention, the signal peptide selected from the peptides having the amino acid sequences set forth in SEQ ID NOS: 5-16, 18-19, 21-29, 31-36, 38-42, 45, 48-53, 55, 57-64, 255-304, 381-429 and 476 was obtained and proved to facilitate production of disulfide-stabilized single chain antibody. Accordingly, the preferred isolated nucleic acid encoding each signal peptide as mentioned was also provided.

In one example of the present invention, the anti-VEGF sc-dsFv was developed by using the signal peptides as identified and obtained by the method of the present invention. In another example, anti-H5 sc-dsFv against influenza virus was developed (see FIG. 5).

In order to confirm the formation of disulfide bond in the phage-displayed sc-dsFv variants of the present invention, a fXa substrate sequence (-IEGR-) in the linker sequence between the two variable domains was constructed. As shown in FIG. 4, without the fXa treatment, both anti-VEGF scFv (fXa+) and scFv(fXa-) bound to immobilized VEGF. In contrast, with the fXa treatment, only the anti-VEGF scFv(fXa-)

bound to immobilized VEGF. The cleavage of the fXa substrate sequence in the phage-displayed anti-VEGF scFv (fXa+) resulted in separation of the variable domains, which in turn abolished the affinity of the phage-displayed scFv against immobilized VEGF. The anti-VEGF scFv(fXa-) was quite insensitive to the treatment of fXa, indicating that no other fXa substrate sequences exist in the displayed protein.

Unexpectedly, it was found in the present invention that each of the signal peptides having the amino acid sequences of SEQ ID NOS: 5-593 as listed in Tables 2-4 enabled the expression and proper folding of the sc-dsFv structure on the phage-displayed platform. In addition, they resulted in secretion of the soluble non-fusion sc-dsFv in culture media.

Accordingly, the present invention also provides a method for producing a disulfide-stabilized single chain antibody. The method includes providing a host cell containing an expression construct, and culturing the host cell in a medium under conditions allowing expression of the disulfide-stabilized single chain antibody. The expression construct includes a first nucleotide sequence encoding a signal peptide, and a second nucleotide sequence encoding a single 20 chain antibody capable of forming an interface disulfide bond. The second nucleotide sequence is located 3' downstream to the first nucleotide. The signal peptide has the amino acid sequence of:

(a) 25 strating that infl VKKLL $X_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}$ AAQPAMAHHHH HHGH (SEQ ID NO:596), in which X_1 is A, C, F, G, I, L, M, P, Q, S, V, W, or Y; X_2 is A, D, F, G, H, I, L, M, N, P, S, T, V, or W; X_3 is A, F, G, L, M, P, Q, R, S, T, V, W, or Y; X_5 is A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X_6 is A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X_6 is A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X_6 is A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; X_6 is A, C, D, E, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; X_6 is A, C, D, E, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; X_6 is A, C, D, E, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; and X_{10} is A, C, D, E, F, G, H, IHUMAN VECTOR Human VECTOR 100 in the control of the c

 $\begin{array}{l} \text{(B)} \\ \text{VKKLLFAIPLX}_{1} X_{2} X_{3} X_{4} X_{5} X_{6} X_{7} X_{8} X_{9} X_{10} \text{MAHHHH} \\ \text{HHGH (SEQ ID NO:597), in which } X_{1} A, C, F, G, H, I, L, M, \\ \text{N, P, Q, S, T, V, W, or Y; } X_{2} \text{ is A, C, D, F, G, H, I, L, M, P, Q, 40} \\ \text{R, S, T, V, W, or Y; } X_{3} \text{ is A, C, D, F, G, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; } X_{4} \text{ is A, C, E, F, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; } X_{5} \text{ is A, C, D, F, H, I, L, M, N, P, Q, R, S, T, V, W, or Y; } X_{6} \text{ is A, C, D, E, F, G, H, K, L, M, P, Q, R, S, T, V, W, or Y; } X_{7} \text{ is A, D, E, F, G, H, K, L, M, N, P, Q, R, S, T, V, or Y; } X_{8} \text{ is A, C, F, G, I, K, L, M, N, P, Q, R, S, T, or V; } X_{9} \text{ is A, C, D, E, F, G, H, K, L, M, N, P, Q, R, S, T, or V; } X_{9} \text{ is A, C, D, E, F, G, H, L, M, N, P, Q, R, S, T, or V; } x_{9} \text{ is A, C, D, E, F, G, H, L, M, N, P, Q, R, S, T, V, W, or Y; } x_{1} \text{ or A} X_{10} \text{ is A, C, D, E, F, G, H, L, M, P, Q, R, S, or T; } x_{1} \text{ or A} X_{2} \text{ or A} X_{3} \text{ or A} X_{4} \text{ or A}$

VKKLLFAIPLVVPFYX₁X₂X₃X₄X₅X₆X₇X₈X₉X₁₀HH
HGH (SEQ ID NO:598), in which X₁ is A, C, D, F, G, I, L, M,
N, P, Q, R, S, T, V, or Y; X₂ is A, C, D, F, G, H, K, L, N, P, Q,
R, S, T, V, W, or Y; X₃ is A, C, E, F, G, H, I, K, L, M, N, P, Q, R,
S, T, V, W, or Y; X₄ is A, C, D, F, G, H, I, L, M, N, P, Q, R,
S, T, V, W, or Y; X₅ is A, C, E, F, G, H, I, K, L, M, N, P, Q, R,
S, T, V, W, or Y; X₆ is A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R,
S, T, V, W, or Y; X₇ is A, D, E, F, G, H, I, K, L, M, N, P, Q, R,
S, T, V, or Y; X₈ is A, E, F, G, H, I, K, L, M, N, P, Q, R, S, T,
V, W, or Y; X₉ is A, D, F, G, H, I, K, L, M, N, P, Q, R, S, T,
V, W, or Y; and X₁₀ is A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, 60
T, V, or Y.

Similar to the aforementioned experiment, the extent (percentage) of the interface disulfide bond formation of the sc-dsFv from the optimum signal sequence variants from L4 were tested. As shown in FIG. **6**A, signal sequence optimization could improve the disulfide bond formation in the sc-dsFv from ~0% up to 40% of the secreted sc-dsFv molecule.

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As shown in FIG. **6**B, the interface disulfide bond formation enhanced the affinity for the sc-dsFv-VEGF interaction.

In the present invention, a stability test of soluble sc-dsFv was conducted. As shown in FIGS. 7A and 7B, the sc-dsFv antibody fragment scaffold was indeed substantially more stable than the scFv scafold due to the interface disulfide bond in the sc-dsFv constructs.

According to the invention, the concentration of sc-dsFv antibody produced by the method disclosed herein was unexpectedly high, and stable. Thus, the present invention provides the sc-dsFv at a high concentration sufficient for coating on a solid phase to produce an array for detection or diagnosis without aggregation, different from the prior art where sc-Fv tends to precipitate under the same concentration due to aggregation.

Accordingly, the present invention provides an array of disulfide-stabilized single chain antibodies produced by the aforementioned method coated on a solid phase. In one example of the invention, the solid phase may be made from silicon, plastic, nylon, glass, ceramic, photoresist or rubber. In one embodiment of the present invention, a microarray test was established using the disulfide-stabilized single chain antibodies produced by the method of the invention, demonstrating that influenza virus could successfully be detected by an array of a serious dilution of anti-H5 sc-dsFv coated on a glass.

The present invention is further illustrated by the following examples, which are provided for the purpose of demonstration rather than limitation.

EXAMPLES

Preparation 1: VEGF Expression and Purification—Human VEGF-121

Human VEGF-121 (VEGF-A residue 34-135 receptor binding domain) (Fuh, G. et al., (2006) *J. Biol. Chem.*, 281, 6625-6631) was expressed in *E. coli* as inclusion body. The refolding and purification of VEGF-A were carried out as described in Chang, H. J., et al., (2009) *Structure*, 17, 620-631

Preparation 2: Phage Display Libraries with Diversified Signal Sequences N-terminal to the sc-dsFv-pIII Fusion Protein

45 Phage display libraries with diversified sequences in the signal peptide region N-terminal to the sc-dsFv-pIII fusion protein were constructed with pCANTAB5E phagemid (GE-Amersham Biosciences) as shown in FIG. 1. Primers encoded with the sequence diversification shown in FIG. 1 were syn-thesized by IDT (Integrated DNA Technologies).

For each of the phage display libraries, phagemid templates were constructed with TAA stop codons inserted in the sequence region for diversification (Huang et al., (2010) J. Biol. Chem., in press). The M13pIII-pelB signal sequence for phage-displayed pIII-fusion protein is a combination of the wild-type M13 signal peptide N-terminal to gene III (MKKLLFAIPLVVPFYSHS) (SEQ ID NO:594) and the pelB signal sequence of Pectobacterium wasabiae (MKY-LLPTAAAGLLLLAAQPAMA) (SEQ ID NO:595). This merged signal sequence (shown in bold font above) was considered containing the tentative n- h- and c-regions of the signal sequence. DNA libraries were constructed to diversify the amino acid sequence in the key regions. Each of the four of DNA libraries (L2, L3, L7) contained ten consecutive NNK (N stands for 25% of G, C, A, and T, and K stands for 50% of G and T; underlined by dashed lines) degenerate codons covering a portion of the tentative signal sequence.

Also shown in the Figure are the sequences containing TAA stop codons (underlined regions) used as the templates for the library constructions. The oligonucleotide-directed mutagenesis procedure initially proposed by Kunkel (Kunkel et al., (1987) Methods Enzymol, 154, 367-382) was used for the 5 phagemid library construction. The TAA stop codons in the phagemid templates ensure that the un-mutated phagemid templates after the mutagenesis procedure are incapable of producing pIII fusion protein for phage surface display (Sidhu and Weiss, (2004) Constructing phage display librar- 10 ies by oligonucleotide-directed mutagenesis. In: Clackson, T., and Lowman, H. B. (eds). Phage Display, 1st Ed., Oxford University Press, New York).

After the oligonucleotide-directed mutagenesis procedure, E. coli strand ER2738 was transformed with the phagemid 15 libraries and the recombinant phage particles were rescued with helper phage M13KO7 (GE-Amersham Biosciences). The phage particles were precipitated with PEG/NaCl, and resuspended in PBS. More details of the phage library preparation can be found in a previous publication (Hsu, H. J. et al., 20 (2008) J Biol Chem 283(18), 12343-12353).

Seven sc-dsFv variants were constructed on the basis of the phagemid encoding the template anti-VEGF scFv(fXa+): S1(L: Gln38Cys & H:Gln39Cys); S2(L:Gly41Cys & H:Gly42Cys); S3(L:Ala43Cys & H:Gln112Cys); S4(L: 25 Formation in Phage-displayed Anti-VEGF sc-dsFv Phe98Cys & H:Leu45Cys); S5(L:Gln100Cys H:Gly44Cys); S6(L:Gln38Cys & H:Leu45Cys); S7(L: Ala43Cys & H:Gln112Cys & L:Gln100Cys & H:Gly44Cys). These cysteine pairs were determined by distance constrain for possible disulfide bonds in the model structure (PDB 30 code: 2FJG).

Preparation 3: Biopanning Against VEGF with Phage-displayed Anti-VEGF sc-dsFv Libraries

Maxisorb Immune Tubes (Nunc) were coated with VEGF (25 μg in 1 ml PBS in each tube) at 4° C. overnight. The tubes 35 were blocked with 4 ml of 5% skim milk in PBST (PBS with 0.05% Tween 20) for one hour at room temperature with gentle shaking and then washed with PBST. In each of the tubes, 10¹¹ colony-forming units (cfu) of phage from each of the phage display libraries were mixed with 1 ml of 5% skim 40 milk. The phage particles were allowed to bind to the immobilized VEGF in the tube at room temperature for two hours under gentle shaking. After the binding, the tubes were washed 10 times with PBST and 2 times with PBS. One milliliter of E. coli strand ER2738 in the log phase was added 45 to each of the tubes at room temperature with gentle shaking for 15 minutes. From each tube, the infected E. coli was transferred to 10 ml of a 2YT medium containing 20 µg/ml of ampicillin and was titered with 2YT agar plates containing 100 μg/ml of ampicillin. The infected E. coli was incubated at 50 37° C. for one hour with vigorous shaking. Ampicillin was then added to reach final concentration of 100 µg/ml. The culture was incubated for another hour at 37° C. before transferred to final 100 ml 2YT medium (100 μg/ml of ampicillin) containing 10¹¹ cfu M13KO7 helper phage. After two hours 55 of incubation, kanamycin was added to final concentration of 70 μg/ml. The culture was incubated at 37° C. overnight with vigorous shaking. The phage in the supernatant of the culture was harvested by centrifugation. The phage was titered, precipitated with PEG/NaCl, and resuspended in PBS. The 60 phage solution was ready for the next round of selection.

Preparation 4: Enzyme-linked Immunosorbent Assay (ELISA) for Phage-displayed Anti-VEGF Sc-dsFv Binding Against Immobilized VEGF and Anti-E-tag Antibody

Single E. coli colonies harboring the selected phagemids 65 were randomly picked using a GENETIX Qpix II colony picker to 96-well deep well culture plates. Each well con14

tained 960 μ l 12YT (100 μ g/ml of ampicillin and 10 μ g/ml of tetracyclin). The culture plates were incubated at 37° C. shaking vigorously for 4 hours before adding 20 µl of M13KO7 helper phage (10¹¹ cfu/ml). The plates were then incubated at 37° C. for one hour with vigorous shaking before adding 20 ul of kanamycin to the final concentration of 50 µg/ml. After overnight incubation at 37° C. with vigorous shaking, the cultures were centrifuged at 3000 g for 10 minutes at 4° C. From each well of the culture plates, 100 µl of the supernatant was mixed with 100 µl of 5% skim milk. Half of the phage mixture was added to a corresponding well of a 96-well Maxisorb microtiter plate precoated with VEGF (1 µg/well) and blocked with 5% skim milk; the other half was added to a corresponding well of another microtiter plate precoated with polyclonal goat anti-E-tag antibody (1 μg/well, Novus Biologicals). After one hour incubation at room temperature, the ELISA plates were washed six times with PBST. The phage particles remained on the plates were measured with HRP-labeled mouse anti-M13 antibody (1/3000, GE Healthcare) and TMB substrate (KPL). The reaction was stopped with 50 µl of 1 N HCl and the signal intensity was measured at OD 450 nm.

Preparation 5: Measurement of Interface Disulfide Bond

Fifty microliters of a freshly prepared phage supernatant (see above) was mixed with 50 µl of a two-fold concentrated reaction buffer containing 1 unit of bovine factor Xa (fXa) (Novagen) in a Maxisorb microtiter plate precoated with VEGF (1 µg/well) and blocked with 5% skim milk. After two hours of enzymatic reaction at 37° C., the phage particles remained bound to the microtiter plate were measured following the same ELISA procedure as described above.

Preparation 6: Western Blot Assay for the Phage-displayed Anti-VEGF Sc-dsFv

Single colony phage was amplified, harvested, precipitated with PEG/NaCl, and resuspended in PBS (see above). Phage particles (10¹¹ cfu) were prepared under either a non-reducing or reducing condition before electrophoresis in a 10% SDS-polyacrylamide gel. After the electrophoresis, the proteins in the gel were transferred onto a polyvinylidene fluoride (PVDF) membrane (Millipore). The membrane was blocked with 5% skim milk for 1 hour at room temperature and then incubated with a monoclonal mouse anti-pIII antibody (1/3000 mg/ml, New England Biolabs) for one hour at room temperature. After three washes (5 minutes each) with PBST, the membrane was incubated with HRP-labeled antimouse antibody (1/3000, GE Healthcare) for 1 hour at room temperature. After three washes with 10 ml PBST, the membrane was developed with 4-chloro-1-naphthol (4CN) substrate (KPL) until the desired color intensity was achieved.

Preparation 7: Preparation of Non-fusion Soluble scFv/ScdsFv

Seven hundred and fifty microliters of mid-log phase (OD_{600 nm}=0.6) E. coli host (non-suppressor strain HB2151 or suppressor strain ER2738) grown in a 2YT medium (16 g/L tryptone, 10 g/L yeast extract, 5 g/L NaCl, pH 7.0) was infected with 50 µl of a phage solution (1011 cfu/ml). After one hour incubation at 37° C. with shaking, $100\,\mu l$ ampicillin in a 2YT medium was added to the final concentration of 100 μg/ml. After another hour of incubation, 100 μl isopropylbeta-D-thiogalactopyranoside (IPTG) in a 2YT medium was added to the final concentration of 1 mM. The culture was kept at 37° C. with vigorous shaking overnight. The secreted soluble scFv or sc-dsFv in the supernatant was separated from the bacterial host by centrifugation at 3000 g for 10 minutes.

Preparation 8: ELISA for Immobilized VEGF Binding For phage ELISA, each well in a Maxisorb 96-well microtiter plate (Nunc) was coated with 2 µg VEGF at 4° C. overnight. The wells were blocked with 5% skim milk in PBST (137 mM NaCl, 2.7 mM KCl, 10 mM Na₂HPO₄, 2 mM KH_2PO_4 , 0.1% tween 20, pH 7.4) for one hour. After $3\times300\,\mu$ l PBST and 2×300 ul PBS washes, 100 ul of a phage solution and 100 µl of 5% skim milk in PBST were added to each well and incubated at room temperature with shaking for one hour. After washing each of the wells three times with 300 µl of PBST each and twice with 300 µl of PBS each, the bound phages were labeled with anti-M13 antibody conjugated with HRP (GE-Amersham) 1/3000 dilution in 5% skim milk in PBST for one hour. The ELISA signal was developed by incubating each well with 100 µl of a TMB solution (KPL Inc.) for 5 minutes. The reaction was stopped with 100 µl N HCl, and the optical density was recorded with VICTOR3 Multilabel Plate Readers (Perkin Elmer) at 450 nm.

For scFv or sc-dsFv ELISA, 100 μ l of a soluble scFv $_{20}$ solution was used instead of phage solution, and HRP-conjugated protein L (0.5 μ g/ml in 5% skim milk in PBS, from Pierce) was used instead of HRP-conjugated anti-M13 anti-body. When needed, the ELISA signals were normalized with the signals of the control anti-VEGF scFv in serial dilution. 25

Preparation 9: fXa Protease Digestion

For phage solutions, $20\,\mu l$ (1 unit) of bovine factor Xa (fXa) protease (Novagen) in a six-fold concentrated reaction buffer was added to $100\,\mu l$ of a phage solution at 37° C. After 2 hours of enzymatic reaction, $100\,\mu l$ of 5% skim milk in PB ST was added to the reaction mixture before the VEGF-binding ELISA measurement was carried out in the manner described in the previous section. The fXa resistance percentage was calculated with the ratio of the ELISA reading in the presence of fXa over the ELISA reading in the absence of fXa. The ELISA readings for the ratio were adjusted by shift the baseline determined with the null control ELISA readings. For soluble scFv/sc-dsFv fXa digestion, all procedures were the same except that the enzymatic reaction was carried out for one hour at room temperature.

Preparation 10: Construction of Anti-H5 sc-dsFv Against Influenza Virus

The construction of scFv library derived from mouse spleen after immunization of hemagglutinin from influenza 45 virus was based on the protocols described in "Phage Display, A Laboratory Manual, edited by Carlos F. Barbas III, Dennis R. Burton, Jamie K. Scott, and Gregg J. Silverman, 2001, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., USA". In brief, after hemagglutinin immunization, the 50 total RNA derived from mouse spleen was purified by Trizol reagent (Invitrogen) according to the manufacturer's protocols. After cDNA synthesis by reverse transcriptase, the gene fragments encoded heavy and light chains of antibody variable region were amplified by the specific primer sets 55 described in the book mentioned above, respectively. The scFv fragments were synthesized by two-steps PCR reactions, and then cloned into a pCANTAB 5E phagemid vector with the signal sequence derived from the library 2 for scdsFv phage production. The library complexity was 4.5×10^7 . 60 After panning against H5, two clones were selected for monospectral binding to H5 (clone 8a) and broad spectral binding to H1, H3 and H5 (clone 12a). These two clones were subjected to disulfide bond formation mutants between L100 and H44 (based on Kabat numbering) and then for sc-dsFv phage 65 production and ELISA detection (8aS5 and 12aS5, respectively).

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Preparation 11: Microarray Test for sc-dsFv Binding of H5 Influenza Virus

The just-described sc-dsFv ds-8a or and ds-12a was subcloned into a pET32a vector with thioredoxin as a fusion protein partner at the N-terminus. The thioredoxin-sc-dsFv fusion proteins could be expressed in Rosetta-gami B strain of E. coli in a soluble form. After purification and TEV protease digestion to remove thioredoxin, the purified ds-8a protein was found to have a binding affinity and specificity similar to those of H5 based on an ELISA assay and array studies. The protein ds-AV1, ds-12a and ds-8a were spot on glass slides coated with streptavidin as the purified ds-AV1, ds-12a and ds-8a proteins contained a biotinylated Avitag sequence at their C-termini. The highest protein concentration used for this protein array was 8 mg/ml, 8 mg/ml, and 0.8 mg/ml, respectively. These proteins were 2 fold dilution with a 100 mM sodium phosphate buffer, pH 8.5 from the highest protein concentration for 15 times for spotting (10n1/spot), and then the protein of each concentration was spotted for 5 replicates. After spotting, each glass slide was sealed to form 16 distinct squares for reaction. After blocking with 5% BSA for 30 minutes, the H5 influenza virus (about ~10⁷ PFU/ml) was added to react with spotted sc-dsFvs for 30 minutes. After 3 times wash with a phosphate buffer for 5 minutes each, 40 nm fluorescence beads coated with ds-8a ($\sim 10^7$) were added to each square and incubated for 30 minutes. After 3 times wash again with a phosphate buffer for 5 minutes each, the glass array was air-dried for detection.

Example 1

Selection of Signal Sequences for Effective Expression of Anti-VEGF sc-dsFv on M13 Phage Surface

Phage display libraries L2, L3, and L4 were constructed to diversify the signal sequence of the S5 anti-VEGF sc-dsFv-pIII fusion protein as shown in FIG. 1. The complete DNA construct and the amino acid sequence of the S5 anti-VEGF sc-dsFv are shown in FIG. 1. The S5 sequence remained unchanged in all the variants from the libraries. The complexities of the L2, L3, and L4 phage display libraries were 3.1×10°, 3.7×10°, and 1.5×10°, respectively. These libraries were designed to diversify the signal peptide sequences in the h-region, c-region, and a few N-terminal residues of the mature phage-displayed anti-VEGF sc-dsFv.

Each of the phage display libraries was selected for binding against immobilized VEGF. The trends of enrichment of the VEGF-binding phage variants from each of the three libraries, plotted as functions of the number of selection/amplification cycle, are shown in FIG. 2. After four rounds of selection/amplification cycle, the VEGF-binding phage variants were enriched for more than one order of magnitude. The enrichment trends were similar among the variants from the three libraries. This result indicates that the signal sequence regions covered by the three signal sequence libraries (FIG. 1) could all be optimized to increase the expression of the correctly folded anti-VEGF sc-dsFv on phage surface.

Example 2

Interface Disulfide Bond Formation in Anti-VEGF sc-dsFv on M13 Phage Surface

In order to test the formation of the disulfide bond in the phage-displayed sc-dsFv variants, we constructed two control phage-displayed anti-VEGF scFv variants: one with a

factor Xa cutting site, -IEGR- (SEQ ID NO:599), encoded in the linker peptide connecting the two variable domains (anti-VEGF scFv(fXa+)); the other without this fXa cutting site (anti-VEGF scFv(fXa-)). As shown in FIG. 3, the S5 anti-VEGF sc-dsFv was constructed with a fXa substrate 5 sequence (-IEGR-) in the linker sequence between the two variable domains. The cleavage of the fXa substrate sequence in the phage-displayed anti-VEGF scFv(fXa+) resulted in separation of the variable domains, which in turn abolished the affinity of the phage-displayed scFv against immobilized 10 VEGF. Both phage-displayed scFv's did not have the engineered interface disulfide bond as in S5; the scFv(fXa+) construct had the -IEGR- (SEQ ID NO:599) site in the linker peptide (-(G)₄SIEGRS(G)₄S-) (SEQ ID NO:600), while the scFv(fXa-) construct had the conventional $-(G)_4S(G)_4S(G)$ 15 ₄S- (SEQ ID NO:601) linker peptide.

As shown in FIG. 4, without the fXa treatment, both anti-VEGF scFv(fXa+) and scFv(fXa-) bound to immobilized VEGF. But with the fXa treatment, only the anti-VEGF scFv (fXa-) bound to immobilized VEGF. In contrast, all the S5 20 signal sequence variants for the phage-displayed sc-dsFv showed substantial increase in resistance to fXa protease activity, indicating that the interface disulfide bonds in the anti-VEGF sc-dsFv's were formed to stabilize the functional dimeric structure after the cleavage of the peptide linker 25 between the two variable domains. The results unambigu18

ously demonstrated that the engineered interface disulfide bond was correctly formed in the phage-displayed S5 anti-VEGF sc-dsFv from some of the signal sequence variants from all three VEGF-binding enriched signal sequence libraries (L2, L3 and L4).

Example 3

Preference Sequence Patterns of the Optimum Signal Peptides in Effective Expression of Functional Anti-VEGF sc-dsFv

The functionality of the anti-VEGF sc-dsFv on phage surface was quantified with two quantitative measurements: the affinity of the sc-dsFv against VEGF and the extent of the interface disulfide bond formation. After the tests, 250, 126, and 213 optimum signal sequences were found in L2, L3, and L4 library, respectively, which are summarized as following Tables 2-4. Among them, fifty signal sequence variants with the highest sc-dsFv-VEGF binding affinities selected from more than 3000 random single colonies of the enriched libraries L2, L3, and L4 were marked with the symbol "*." The symbol "q" indicated that the nucleotide sequence TAG (amber stop codon) that could be translated to Gln (Q) with 0.8~20% in *E. coli* amber suppressor strains which were normally used in phage production.

TABLE 2

Pref	Preference sequence patterns selected from L2 S5 sc-dsFv library					
No.	Code	Se	quence	SEQ ID NO:		
	M13-pelB	VKKLL FAIPLVVPFY	ААОРАМАННННН	4		
1	1.12B	VKKLL VLSHLPFMTD	ААОРАМАННННН *	5		
2	9.26.10B	VKKLL SHWLLSSqLQ	ААОРАМАННННН *	6		
3	2.12A	VKKLL AMSLAPSVFP	ААОРАМАННННН *	7		
4	9.12A	VKKLL WSLFFqqLNP	ААОРАМАННННН *	8		
5	2.12F	VKKLL LLSLLQRPLP	ААОРАМАННННН *	9		
6	1.2H	VKKLL LSSWLMTRFP	ААОРАМАННННН *	10		
7	6.9G	VKKLL VLSHFPAFVP	ААОРАМАННННН *	11		
8	1.8F	VKKLL PLLSLPLPPN	ААОРАМАННННН *	12		
9	7.1B	VKKLL VLTPMHFSSP	ААОРАМАННННН *	13		
10	9.26.10A	VKKLL ILALPQSYPL	ААОРАМАННННН *	14		
11	5.4A	VKKLL qALYFSLPSS	ААОРАМАННННН *	15		
12	YJ2.2	VKKLL VSAMTSASFP	ААОРАМАННННН *	16		
13	5.2F	VKKLL LPASWLFGQP	ААОРАМАННННН	17		
14	10.2D	VKKLL WSLFFqqLNP	ААОРАМАННННН *	18		
15	YJ2.34	VKKLL FVMALRSSAP	ААОРАМАННННН *	19		
16	3.3F	VKKLL FLWPFYNGHI	ААОРАМАННННН	20		
17	4.1A	VKKLL QSFYLSLqLD	ААОРАМАННННН *	21		
18	10.7H	VKKLL SLTFPFTIHS	ААОРАМАННННН *	22		
19	1.9D	VKKLL WPVLSPSLFP	ААОРАМАННННН *	23		
20	5.12D	VKKLL PWLFSTFPSS	ААОРАМАННННН *	24		
21	1.8D	VKKLL IMSSLPTLSP	ААОРАМАННННН *	25		

TABLE 2 -continued

	TABLE 2 -continued					
Pref	erence	sequence patterns sel	ected from L2 S5	sc-dsFv library		
No.	Code	Se	quence	SEQ ID NO:		
22	4.11F	VKKLL IMSRVLAPDF	ААОРАМАННННН *	26		
23	1.7C	VKKLL FDFWFSSFLq	ААОРАМАНННННН *	27		
24	4.8G	VKKLL YGqLMLLSSD	ААОРАМАННННН *	28		
25	4.4E	VKKLL PWLFPFHAYP	ААОРАМАННННН *	29		
26	1.12G	VKKLL LVMTLSRQPF	ААОРАМАННННН	30		
27	4.8A	VKKLL ASAYLYHGLS	ААОРАМАНННННН *	31		
28	4.4C	VKKLL PFFAGVLqHP	ААОРАМАНННННН *	32		
29	3.11A	VKKLL ALSSPFFHIP	ААОРАМАНННННН *	33		
30	10.3F	VKKLL PTRqPMMYPP	ААОРАМАНННННН *	34		
31	YJ2.15	VKKLL QLLMPFLNSP	ААОРАМАНННННН *	35		
32	9.9H	VKKLL CSLGYACIPP	ААОРАМАНННННН *	36		
33	4.9C	VKKLL LMPWLFNSPP	ААОРАМАННННН	37		
34	3.12B	VKKLL LDqLAYAALS	ААОРАМАНННННН *	38		
35	4.10G	VKKLL qSTVFFSWLS	ААОРАМАНННННН *	39		
36	YJ2.18	VKKLL LPWALSHQVL	ААОРАМАНННННН *	40		
37	7.2E-q	VKKLL ALTYPAFLYD	ААОРАМАНННННН *	41		
38	1.11A	VKKLL AMAPPMMSMN	ААОРАМАНННННН *	42		
39	5.3D	VKKLL WWSSLFAPSP	ААОРАМАННННН	43		
40	4.6H	VKKLL GSFILARSMD	ААОРАМАННННН	44		
41	5.11C	VKKLL MVLTSWHPYP	ААОРАМАНННННН *	45		
42	2.8C	VKKLL FSLRFFFPSS	ААОРАМАННННН	46		
43	2.5F	VKKLL WLWSTPLFPH	ААОРАМАННННН	47		
44	2.2A	VKKLL PLLFSLDGDP	ААОРАМАНННННН *	48		
45	3.2C-d	VKKLL SVSLSSYSFY	ААОРАМАНННННН *	49		
46	3.1H	VKKLL LNGTESAqLF	ААОРАМАННННН *	50		
47	6.4A	VKKLL WHVLPYLPNS	ААОРАМАНННННН *	51		
48	4.10E	VKKLL SIVPLFSPqS	ААОРАМАННННН *	52		
49	7.4H	VKKLL VMTSPMLAPG	ААОРАМАННННН *	53		
50	2.5H	VKKLL VLSLPSIAPH	ААОРАМАННННН	54		
51	6.4E	VKKLL qSLLLLRALL	ААОРАМАНННННН *	55		
52	2.1A	VKKLL FSLPVFFDLP	ААОРАМАННННН	56		
53	4.11D	VKKLL LLFSMARPLP	ААОРАМАНННННН *	57		
54	7.10A	VKKLL TqAVFPFTFN	ААОРАМАНННННН *	58		
55	3.2E	VKKLL LASWLFRADM	ААОРАМАННННН *	59		
56	5.2E	VKKLL PFLFPFPSPS	ААОРАМАНННННН *	60		
57	YJ2.12	8 VKKLL ALSAWSLSQT	ААОРАМАНННННН *	61		
58	4.7H	VKKLL ALLPLFPTqH	ААОРАМАНННННН *	62		
59	2.10F	VKKLL AALASFPPAP	ААОРАМАНННННН *	63		

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TABLE 2 -continued

Pref	erence sequ	ience patterns sel	ected from L2 S5	sc-dsFv library
No.	Code	Sec	quence	SEQ ID NO:
60	YJ2.22	VKKLL LLMPFLNQSP	ААОРАМАННННН *	64
61	7.5A	VKKLL FTSGLKLVPP	ААОРАМАННННН	65
62	6.10F	VKKLL LqPLLSIYLN	ААОРАМАННННН	66
63	4.11B	VKKLL LSSLWSAYMD	ААОРАМАННННН	67
64	2.5C	VKKLL LLGqsLMHFQ	ААОРАМАННННН	68
65	YJ2.25	VKKLL PQLAMSLPSI	ААОРАМАННННН	69
66	10.3H	VKKLL YETMLSSYLY	ААОРАМАННННН	70
67	3.10D	VKKLL SLYYFPLVPY	ААОРАМАННННН	71
68	4.7C	VKKLL qRTVAAAYFW	ААОРАМАННННН	72
69	4.12D	VKKLL FLTWLRYGFP	ААОРАМАННННН	73
70	6.1A	VKKLL LLLTLMqPTS	ААОРАМАННННН	74
71	8.10C	VKKLL FDFFTHVHLF	ААОРАМАННННН	75
72	5.6E	VKKLL ALYPHFVSFT	ААОРАМАННННН	76
73	4.11E	VKKLL LPYAIqLFSP	ААОРАМАННННН	77
74	YJ2.5	VKKLL WFPLHSSLLP	ААQРАМАННННН	78
75	4.7A	VKKLL PALLLATAAF	ААОРАМАННННН	79
76	3.11C	VKKLL LASVAWNLDS	ААОРАМАННННН	80
77	YJ2.121	VKKLL VGSLLFWPQQ	ААОРАМАННННН	81
78	4.5F	VKKLL SPLLFLqNYT	ААОРАМАНННННН	82
79	3.2F	VKKLL SYWLDFIqVL	ААОРАМАНННННН	83
80	10.3C	VKKLL VPSFLLSPSP	ААОРАМАННННН	84
81	9.23.7H	VKKLL SLYWLTSqPL	ААОРАМАННННН	85
82	3.9A	VKKLL FALSSVHSPP	ААОРАМАННННН	86
83	4.11H	VKKLL SYYSLLYSYP	ААОРАМАННННН	87
84	3.1C	VKKLL LVSGLqPWYF	ААОРАМАННННН	88
85	2.5A	VKKLL VLATPLHLSP	ААОРАМАННННН	89
86	10.6H-q	VKKLL SLAFPLFTPP	ААОРАМАННННН	90
87	3.6A	VKKLL SLVPIFPFST	ААОРАМАННННН	91
88	8.10D	VKKLL qPVLFSFFIR	ААОРАМАННННН	92
89	4.3B	VKKLL MSqFLNLLSP	ААОРАМАННННН	93
90	2.3G	VKKLL WAVqPLFPLN	ААОРАМАННННН	94
91	5.3H	VKKLL MFSLVPSPPI	ААОРАМАННННН	95
92	10.7B	VKKLL PFFLQPFqFP	ААОРАМАННННН	96
93	7.2D-q	VKKLL PDLLASVLPV	ААОРАМАННННН	97
94	2.9H	VKKLL FWqFLWPSLP	ААОРАМАННННН	98
95	6.4A	VKKLL LLGqFFPNPM	ААОРАМАННННН	99
96	6.4D	VKKLL TLSALSQWHP	ААОРАМАННННН	100
97	9.4D	VKKLL SLVYFFPFYP	ААОРАМАННННН	101

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TABLE 2 -continued

	TABLE 2 -continued					
Pref	Preference sequence patterns selected from L2 S5 sc-dsFv library					
No.	Code	Sec	quence	SEQ ID NO:		
98	10.2H	VKKLL FAFAPAPFYH	ААОРАМАННННН	102		
99	4.12B	VKKLL FLPFALVPRQ	ААОРАМАННННН	103		
100	4.1F	VKKLL ALWMqLYPQD	ААОРАМАННННН	104		
101	YJ2.27	VKKLL ASILFSHAAP	ААОРАМАННННН	105		
102	2.2C	VKKLL LPLPWSLHLY	ААОРАМАННННН	106		
103	4.9C	VKKLL LPHFMSFWFE	ААОРАМАННННН	107		
104	7.3E	VKKLL LFQPFWPIPY	ААОРАМАННННН	108		
105	4.7F	VKKLL LLFSLGRLPP	ААОРАМАННННН	109		
106	7.12G	VKKLL PLWVLLKDPL	ААОРАМАННННН	110		
107	9.3B	VKKLL MSFATLFPHN	ААОРАМАННННН	111		
108	4.5B	VKKLL qHSLVTSWLC	ААОРАМАННННН	112		
109	5.2H	VKKLL LLFqGAFVGq	ААОРАМАННННН	113		
110	4.4C	VKKLL WMFHSLPFSP	ААОРАМАННННН	114		
111	6.8G	VKKLL LTqLLLTRLH	ААОРАМАННННН	115		
112	4.10A	VKKLL ALTLVPSSYP	ААОРАМАННННН	116		
113	4.5D	VKKLL LPWYMLLSDS	ААОРАМАННННН	117		
114	9.3E	VKKLL VVTqFWPSLP	ААОРАМАННННН	118		
115	4.3G	VKKLL LSTLFLWHVR	ААОРАМАННННН	119		
116	9.7E	VKKLL RSLFFqqLYP	ААОРАМАННННН	120		
117	YJ2.30	VKKLL TLTTLHQTFP	ААОРАМАННННН	121		
118	1.3B	VKKLL SALLAPWYWD	ААОРАМАННННН	122		
119	8.9B	VKKLL AIqqRMQIYT	ААОРАМАННННН	123		
120	3.4E	VKKLL LLFPWFQPPY	ААОРАМАННННН	124		
121	9.23.7E	VKKLL YFTSLLGqFP	ААОРАМАННННН	125		
122	6.3D	VKKLL PVLIFLSEIR	ААОРАМАННННН	126		
123	9.5G	VKKLL VATSLRWAVT	ААОРАМАННННН	127		
124	YJ2.54	VKKLL AQLFHLFATH	ААОРАМАННННН	128		
125	8.6G	VKKLL LqFSALFNSF	ААОРАМАННННН	129		
126	7.12C-q	VKKLL FHLMSMLPPP	ААОРАМАННННН	130		
127	5.4C	VKKLL PVCSqSMFPI	ААОРАМАННННН	131		
128	YJ2.48	VKKLL LLLSSSYQSP	ААОРАМАННННН	132		
129	4.3D	VKKLL LDSLFFHAPL	ААОРАМАННННН	133		
130	7.7A	VKKLL qAWVFSAHQL	ААОРАМАННННН	134		
131	YJ2.99	VKKLL FQALGALTSP	ААОРАМАННННН	135		
132	9.9D	VKKLL CFFFFLqFHP	ААОРАМАННННН	136		
133	4.12F-f	VKKLL CFSHLALPSP	ААОРАМАННННН	137		
134	6.2B	VKKLL FGSWIPFTQM	ААОРАМАННННН	138		
135	4.6F	VKKLL GLGYFNWTLL	ААОРАМАННННН	139		

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TABLE 2 -continued

TABLE 2 -continued						
Pref	Preference sequence patterns selected from L2 S5 sc-dsFv library					
No.	Code	Sec	quence	SEQ ID NO:		
136	10.4A	VKKLL HLFPLFQFHH	ААОРАМАННННН	140		
137	5.6B	VKKLL SEHVSSICVL	ААОРАМАННННН	141		
138	3.11E	VKKLL FSCLLDPTCP	ААОРАМАННННН	142		
139	8.3F	VKKLL LYLLHPSFLP	ААОРАМАННННН	143		
140	2.2F	VKKLL WCAPLLYSLR	ААОРАМАННННН	144		
141	2.3F	VKKLL FAMFPYTFqT	ААОРАМАННННН	145		
142	10.5D	VKKLL LPSLFYVESL	ААОРАМАННННН	146		
143	8.8B	VKKLL SLWLSSLSVL	ААОРАМАННННН	147		
144	YJ2.17	VKKLL PHLWFLWSLK	ААОРАМАННННН	148		
145	7.5B	VKKLL ASDPVWYFLW	ААОРАМАННННН	149		
146	10.12D	VKKLL GLPLMGLqSL	ААОРАМАННННН	150		
147	2.4H	VKKLL PQLLLLRALS	ААОРАМАННННН	151		
148	5.5D	VKKLL APSAFSLHLF	ААОРАМАННННН	152		
149	9.4C	VKKLL FqLSSLFVPY	ААОРАМАННННН	153		
150	4.5H	VKKLL VPSFLSTMIE	ААОРАМАННННН	154		
151	2.7B	VKKLL ASPFFASYLW	ААОРАМАННННН	155		
152	YJ2.23	VKKLL LQYLLSPIGY	ААОРАМАННННН	156		
153	6.2D	VKKLL VLSVPISAHH	ААОРАМАННННН	157		
154	7.4A	VKKLL MMqALSSLPE	ААОРАМАННННН	158		
155	4.12B	VKKLL MPAVLATRLT	ААОРАМАННННН	159		
156	6.12E	VKKLL PFTAWIIDGW	ААОРАМАННННН	160		
157	YJ2.125	VKKLL TQLLPLWQPL	ААОРАМАННННН	161		
158	YJ2.21	VKKLL LVPSLLPLTQ	ААОРАМАННННН	162		
159	10.12B	VKKLL PIQSCMVIPS	ААОРАМАННННН	163		
160	YJ2.35	VKKLL WSLHLATRLL	ААОРАМАННННН	164		
161	6.11H	VKKLL qQVLLCSTLR	ААОРАМАННННН	165		
162	7.3B	VKKLL LLRYFLDPMY	ААОРАМАННННН	166		
163	10.12A	VKKLL IPQFLRSHHR	ААОРАМАННННН	167		
164	YJ2.6	VKKLL GVLHLALSLR	ААОРАМАННННН	168		
165	4.12C	VKKLL LVTSqFSLVP	ААОРАМАННННН	169		
166	YJ2.19	VKKLL PLALSWFQLR	ААОРАМАННННН	170		
167	YJ2.88	VKKLL QHQWYPTVLM	ААОРАМАННННН	171		
168	YJ2.29	VKKLL LMYWLSKPLS	ААОРАМАННННН	172		
169	YJ2.8	VKKLL TQLTLSSSPI	ААОРАМАННННН	173		
170	YJ2.94	VKKLL QLTALLSRLI	ААОРАМАННННН	174		
171	YJ2.107	VKKLL LMTFGTTPQS	ААОРАМАННННН	175		
172	YJ2.133	VKKLL SAFSFSLSST	ААОРАМАННННН	176		
173	6.1A	VKKLL APWLVLPHFP	ААОРАМАННННН	177		

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TABLE 2 -continued

- Continued						
Pref	erence sequ	uence patterns sel	ected from L2 S5	sc-dsFv library		
No.	Code	Sec	SEQ ID NO:			
174	YJ2.81	VKKLL HVLSFAPPMP	ААОРАМАННННН	178		
175	YJ2.38	VKKLL NWLFFAHPFS	ААОРАМАННННН	179		
176	YJ2.20	VKKLL QLAVLLGSLR	ААОРАМАННННН	180		
177	7.1D	VKKLL LFGLFYFRAC	ААОРАМАННННН	181		
178	YJ2.98	VKKLL FQFFVVWRLL	ААОРАМАННННН	182		
179	YJ2.39	VKKLL PWAWPPPPFW	ААОРАМАННННН	183		
180	YJ2.130	VKKLL LQLVIVYYLR	ААОРАМАННННН	184		
181	YJ2.16	VKKLL RQSVLLSALH	ААОРАМАННННН	185		
182	3.12E	VKKLL VYGYFLTTFR	ААОРАМАННННН	186		
183	YJ2.53	VKKLL CFSPLFGFHT	ААОРАМАННННН	187		
184	YJ2.100	VKKLL PGYALWQTIP	ААОРАМАННННН	188		
185	YJ2.58	VKKLL QRIFICFFLR	ААОРАМАННННН	189		
186	8.2A	VKKLL PHVFSCqLSA	ААОРАМАННННН	190		
187	5.10A	VKKLL SPLSLSVKLL	ААОРАМАННННН	191		
188	9.2D	VKKLL ARSLFSGSML	ААОРАМАННННН	192		
189	YJ2.92	VKKLL LQFLIVFPLR	ААОРАМАННННН	193		
190	YJ2.32	VKKLL LAVLLGQSLR	ААОРАМАННННН	194		
191	YJ2.14	VKKLL LLSHLFLRLH	ААОРАМАННННН	195		
192	8.4E	VKKLL LAMVFFVTLR	ААОРАМАННННН	196		
193	YJ2.117	VKKLL WLFALPQENV	ААОРАМАННННН	197		
194	YJ2.66	VKKLL HPLVLLSSSP	ААОРАМАННННН	198		
195	YJ2.131	VKKLL LQYLFMLSMR	ААОРАМАННННН	199		
196	4.11H	VKKLL PALLIRYASV	ААОРАМАННННН	200		
197	YJ2.78	VKKLL QQFTSPFLLL	ААОРАМАННННН	201		
198	YJ2.44	VKKLL SPCFFLLYLR	ААОРАМАННННН	202		
199	YJ2.90	VKKLL PGMPLFFTNS	ААОРАМАННННН	203		
200	YJ2.47	VKKLL PQVFFLFRPF	ААОРАМАННННН	204		
201	YJ2.110	VKKLL PFPILLQSPF	ААОРАМАННННН	205		
202	YJ2.74	VKKLL FQACCLFPLQ	ААОРАМАННННН	206		
203	YJ2.55	VKKLL AVVHTMPLFS	ААОРАМАННННН	207		
204	YJ2.108	VKKLL QFSWAFVSIL	ААОРАМАННННН	208		
205	YJ2.96	VKKLL PVCLFWSFFR	ААОРАМАННННН	209		
206	YJ2.70	VKKLL QLLWQQQVPV	ААОРАМАННННН	210		
207	YJ2.60	VKKLL PLQALSWFLR	ААОРАМАННННН	211		
208	YJ2.119	VKKLL FYLLCRLSLQ	ААОРАМАННННН	212		
209	YJ2.82	VKKLL YLQILVICLR	ААОРАМАННННН	213		
210	YJ2.63	VKKLL QLFLIVFPLR	ААОРАМАННННН	214		
211	10.5A	VKKLL PLHFALFFRL	ААОРАМАННННН	215		

TABLE 2 -continued

Pref	erence sequ	uence patterns sel	ected from L2 S5	sc-dsFv library
No.	Code	Sec	quence	SEQ ID NO:
212	YJ2.85	VKKLL PFPMHLVLPF	ААОРАМАННННН	216
213	YJ2.86	VKKLL PLLFSPPSLH	ААОРАМАННННН	217
214	YJ2.126	VKKLL CQSITFSSIW	ААОРАМАННННН	218
215	YJ2.112	VKKLL WQRLFPFLLI	ААОРАМАННННН	219
216	YJ2.77	VKKLL MVPFWPFSFT	ААОРАМАННННН	220
217	YJ2.103	VKKLL QAFPLPPLLV	ААОРАМАННННН	221
218	YJ2.134	VKKLL PLYLLFRSFV	ААОРАМАННННН	222
219	YJ2.91	VKKLL HRSMYLSWLY	ААОРАМАННННН	223
220	YJ2.64	VKKLL LLSTLVRAPY	ААОРАМАННННН	224
221	YJ2.87	VKKLL PLALSQWFLR	ААОРАМАННННН	225
222	YJ2.116	VKKLL AQGMIFFLRL	ААОРАМАННННН	226
223	YJ2.62	VKKLL FCCRLALQFF	ААОРАМАННННН	227
224	YJ2.102	VKKLL YLQFLSLMLS	ААОРАМАННННН	228
225	YJ2.106	VKKLL CQATFPTLLC	ААОРАМАННННН	229
226	YJ2.124	VKKLL ARSYLYFSLS	ААОРАМАННННН	230
227	YJ2.111	VKKLL YQSSFLPLFW	ААОРАМАННННН	231
228	YJ2.104	VKKLL SASFLAFRIT	ААОРАМАННННН	232
229	YJ2.67	VKKLL SVLFLSHYHS	ААОРАМАННННН	233
230	YJ2.105	VKKLL PLALLYVRLS	ААОРАМАННННН	234
231	YJ2.127	VKKLL PEFLLLFRFF	ААОРАМАННННН	235
232	YJ2.80	VKKLL FPSLYAWGGL	ААОРАМАННННН	236
233	YJ2.122	VKKLL LQAAAFFCWL	ААОРАМАННННН	237
234	YJ2.79	VKKLL PFFLFCSSLR	ААОРАМАННННН	238
235	YJ2.115	VKKLL ELTQLWLFHL	ААОРАМАННННН	239
236	YJ2.113	VKKLL PGVPLLLCFR	ААОРАМАННННН	240
237	YJ2.114	VKKLL SQAYLSYFLY	ААОРАМАННННН	241
238	YJ2.61	VKKLL ISYAFLVRVT	ААОРАМАННННН	242
239	YJ2.123	VKKLL APALLRSILA	ААОРАМАННННН	243
240	YJ2.109	VKKLL HSHTLLMSLH	ААОРАМАННННН	244
241	YJ2.83	VKKLL AVSAFVSLVR	ААОРАМАННННН	245
242	YJ2.31	VKKLL TLITFKFLPH	ААОРАМАННННН	246
243	YJ2.49	VKKLL QQFAIPLVEF	ААОРАМАННННН	247
		VKKLL MPCLLVYYLE		248
		VKKLL RYCLLLQIVR		249
		VKKLL SLALLRVSLG		
		VKKLL IIGRIALILR		
∠48	102.24	VKKLL PQLICAFILR	ААСТАПАННННН	252

TABLE 2 -continued

Preference	sequence patterns selected from L2 S5	sc-dsFv library
No. Code	Sequence	SEQ ID NO:
249 8.3E	VKKLL MVPLFPLPLP AAQPAMAHHHHH	253
250 8.1B	VKKLL HGAILYYYLN AAQPAMAHHHHH	254

TABLE 3

Pre	ference se	quence patte	erns selecte	d from L3	S5	sc-dsFv library
No.	Code		Sequence			SEQ ID NO
	M13-pelB	VKKLLFAIPL	VVPFYAAQPA	МАННННН		4
1	2.1A	VKKLLFAIPL	LPAQAMPMSR	МАННННН	*	255
2	7.5C	VKKLLFAIPL	YFVLVRESSS	МАННННН	*	256
3	1.3B	VKKLLFAIPL	VLVVSSRTRA	МАННННН	*	257
4	YJ3.25	VKKLLFAIPL	LLSRPRAVPD	МАННННН	*	258
5	3.8A	VKKLLFAIPL	CVSVRSPAFA	МАННННН	*	259
6	1.6A	VKKLLFAIPL	MTTLASRTHA	МАННННН	*	260
7	1.4H	VKKLLFAIPL	YLSMTRSGAA	МАННННН	*	261
8	7.8F	VKKLLFAIPL	WLRSSVPVDS	МАННННН	*	262
9	7.8H	VKKLLFAIPL	LSSLTRDSSS	манннннн	*	263
10	7.5E	VKKLLFAIPL	GLFTIRDSFA	манннннн	*	264
11	7.60	VKKLLFAIPL	WLGITKPVWS	манннннн	*	265
12	1.3F	VKKLLFAIPL	YTLTPRPVFS	нининим	*	266
13	1.5F	VKKLLFAIPL	qLALSRPSFP	нининим	*	267
14	14.9A	VKKLLFAIPL	SSFLVADQSS	нининим	*	268
15	YJ3.7	VKKLLFAIPL	LLGLASPRSR	МАННННН	*	269
16	13.1E	VKKLLFAIPL	LTLSNRSAWS	МАННННН	*	270
17	2.2C	VKKLLFAIPL	LSLYPTRSTA	МАННННН	*	271
18	YJ3.10	VKKLLFAIPL	LTTLSRPSFS	МАННННН	*	272
19	8.1A	VKKLLFAIPL	YESRPPqPSS	МАННННН	*	273
20	6.2H	VKKLLFAIPL	TMSSPPRSTS	МАННННН	*	274
21	8.1C	VKKLLFAIPL	YFLRISPSAS	МАННННН	*	275
22	1.8B	VKKLLFAIPL	LFLRPSAARP	МАННННН	*	276
23	1.8C	VKKLLFAIPL	LWSSSRPTSQ	нининим	*	277
24	YJ3.41	VKKLLFAIPL	YLVCSRPLHA	МАННННН	*	278
25	10.8G	VKKLLFAIPL	VLQRPPSPNT	нининим	*	279
26	2.7C	VKKLLFAIPL	AMASFRPRDQ	нининнам	*	280
27	7.10C	VKKLLFAIPL	SRSLAMQPLP	нининим	*	281
28	1.2A	VKKLLFAIPL	LSSLRSSNPE	нининим	*	282
29	YJ3.4	VKKLLFAIPL	SILINFRASS	МАННННН	*	283
30	1.6B	VKKLLFAIPL	YWRSFWEPPA	нининнам	*	284

33 TABLE 3 -continued

Pre	ference	sequence patte	erns selecte	d from L3	S5	sc-dsFv lik	orary
No.	Code		Sequence			SEQ ID	NO
31	4.8E	VKKLLFAIPL	YLAAPRSTVA	МАНННННН	*	285	
32	6.7H	VKKLLFAIPL	QYSAFSMSPR	МАННННН	*	286	
33	7.9C	VKKLLFAIPL	YLVSSKNSYP	МАННННН	*	287	
34	YJ3.72	VKKLLFAIPL	GLSVSFRTSA	МАННННН	*	288	
35	4.4C	VKKLLFAIPL	AMLEPTRSSA	МАННННН	*	289	
36	11.1B	VKKLLFAIPL	SLSLHRPALA	МАННННН	*	290	
37	6.6B	VKKLLFAIPL	LSASARGSYA	МАННННН	*	291	
38	YJ3.26	VKKLLFAIPL	YLAVTHRAYS	нининим	*	292	
39	YJ3.44	VKKLLFAIPL	FFSLSRYSLA	МАННННН	*	293	
40	5.4B	VKKLLFAIPL	YLSAPRHASP	манннннн	*	294	
41	5.2D	VKKLLFAIPL	WSFSRLPSSD	нининим	*	295	
42	12.4E	VKKLLFAIPL	YLSLTKPSLS	манннннн	*	296	
43	14.1C	VKKLLFAIPL	SSPATEVLSP	манннннн	*	297	
44	6.2C	VKKLLFAIPL	TLFLQRSSLA	манннннн	*	298	
45	YJ3.6	VKKLLFAIPL	VFTRVPHKPS	манннннн	*	299	
46	4.1E	VKKLLFAIPL	AITRSSQFPS	нининим	*	300	
47	6.4H	VKKLLFAIPL	LGDLRSSPDA	МАННННН	*	301	
48	YJ3.53	VKKLLFAIPL	VTTLSTRCYA	МАННННН	*	302	
49	7.7B	VKKLLFAIPL	FDASLEGPAM	нининим	*	303	
50	11.3C	VKKLLFAIPL	YFSSPSSRAP	нининим	*	304	
51	1.12A	VKKLLFAIPL	WFSFPFRSAA	ниннним		305	
52	12.1A	VKKLLFAIPL	YLSMSSPARS	МАННННН		306	
53	1.12D	VKKLLFAIPL	SWSLCRPVCA	нининим		307	
54	4.3G	VKKLLFAIPL	LYCWPRHSWS	МАННННН		308	
55	YJ3.38	VKKLLFAIPL	IFYTTRSSLS	МАННННН		309	
56	YJ3.45	VKKLLFAIPL	IYTLRSHSMT	МАННННН		310	
57	2.9H	VKKLLFAIPL	PVPSLLGSAD	МАННННН		311	
58	9.5A	VKKLLFAIPL	SLSLNSRSYP	МАННННН		312	
59	2.7H	VKKLLFAIPL	FSPTSQEIRH	МАННННН		313	
60	2.2G	VKKLLFAIPL	YFSCPLRVAS	МАННННН		314	
61	YJ3.81	VKKLLFAIPL	VLSLNRGVFA	МАННННН		315	
62	7.4H	VKKLLFAIPL	SPqVLSSSPG	МАННННН		316	
63	4.2C	VKKLLFAIPL	YVNAMSSPRP	МАННННН		317	
64	13.6D	VKKLLFAIPL	YFTFVRSSWC	МАННННН		318	
65	5.8D	VKKLLFAIPL	FDLSSDSVSP	МАННННН		319	
66	YJ3.47	VKKLLFAIPL	YILFWRNTHA	МАННННН		320	
67	13.7A	VKKLLFAIPL	SCFLSRSAFS	МАННННН		321	
68	YJ3.83	VKKLLFAIPL	FFMITSKSRS	МАНННННН		322	

TABLE 3 -continued

Pre	ference se	quence patte	erns selecte	d from L3 S	55 sc-dsFv library
	Code				SEQ ID NO
69	12.6C	VKKLLFAIPL			
70	4.10B	VKKLLFAIPL	AASRPLSPAA	МАНННННН	324
71	YJ3.46	VKKLLFAIPL	WLFSPLRSYS	МАНННННН	325
72	YJ3.56	VKKLLFAIPL	FLSYVRPLSA	нннннам	326
73	13.5G	VKKLLFAIPL	FIFTPRSVHS	МАНННННН	327
74	2.2E	VKKLLFAIPL	VSSIYKNSPP	МАННННН	328
75	5.5H	VKKLLFAIPL	MSDSTAPSFA	МАННННН	329
76	6.4B	VKKLLFAIPL	TLPqPRFPSP	МАНННННН	330
77	7.10G	VKKLLFAIPL	SLLADSPRRP	МАННННН	331
78	5.3A	VKKLLFAIPL	FTDNSGEPSL	маннинн	332
79	11.1E	VKKLLFAIPL	YCMPMSRTCA	МАНННННН	333
80	11.1D	VKKLLFAIPL	MSRLSYHTPS	ниннинам	334
81	2.2F	VKKLLFAIPL	LSNSRVPPSS	МАНННННН	335
82	15.7A	VKKLLFAIPL	FFASMRHTqA	МАНННННН	336
83	YJ3.5	VKKLLFAIPL	LLSTIKTSFS	нннннам	337
84	3.3A	VKKLLFAIPL	FQQSSLSSVP	МАННННН	338
85	16.11A	VKKLLFAIPL	TLILSHRSSA	МАНННННН	339
86	11.12A	VKKLLFAIPL	SFSRDPSFTS	МАННННН	340
87	9.1B	VKKLLFAIPL	ALSPTRHTLA	МАННННН	341
88	13.9A	VKKLLFAIPL	NILFTVRVYA	МАНННННН	342
89	YJ3.15	VKKLLFAIPL	LASLSARCHG	МАННННН	343
90	12.6B	VKKLLFAIPL	SVTLSLRASA	МАНННННН	344
91	15.8H	VKKLLFAIPL	SHDPLLLSSP	МАНННННН	345
92	YJ3.71	VKKLLFAIPL	LWSLSSRGMT	МАНННННН	346
93	YJ3.82	VKKLLFAIPL	LISYCRPVSS	МАНННННН	347
94	9.1D	VKKLLFAIPL	HSVELPASPA	МАНННННН	348
95	9.6A	VKKLLFAIPL	LLSTSRSSSG	МАННННН	349
96	YJ3.34	VKKLLFAIPL	WFSCSRFALS	МАННННН	350
97	YJ3.28	VKKLLFAIPL	VCTLSSRAFS	МАНННННН	351
98	11.1H	VKKLLFAIPL	YSPLARNPFS	МАНННННН	352
99	16.9D	VKKLLFAIPL	FFAFSRQSSG	МАННННН	353
100	YJ3.70	VKKLLFAIPL	TFSIFSRALA	МАННННН	354
101	YJ3.55	VKKLLFAIPL	SLFFSARAIA	МАНННННН	355
102	9.7A	VKKLLFAIPL	SQPSLCDPVP	МАНННННН	356
103	10.11A	VKKLLFAIPL	LASYHRVAFA	МАНННННН	357
104	10.1F	VKKLLFAIPL	WQLWQLPSRP	МАНННННН	358
105	16.8A	VKKLLFAIPL	FTPMYRPTSP	МАНННННН	359
106	YJ3.27	VKKLLFAIPL	LLSLHRFSFA	МАНННННН	360

37TABLE 3 -continued

Preference	sequence patte	erns selecte	d from L3 S	5 sc-dsFv library
No. Code		Sequence		SEQ ID NO
107 9.5H	VKKLLFAIPL	SYSHPQNALA	МАННННН	361
108 10.12D	VKKLLFAIPL	YVLRSDASWG	НННННАМ	362
109 4.2D	VKKLLFAIPL	FSGPPFDRTS	МАННННН	363
110 YJ3.66	VKKLLFAIPL	FCALSRFTHA	МАННННН	364
111 YJ3.24	VKKLLFAIPL	FSLSRPVPPL	МАННННН	365
112 10.7D	VKKLLFAIPL	SMDSFSRPFF	МАННННН	366
113 15.7C	VKKLLFAIPL	YTIIPSRASS	МАННННН	367
114 15.12C	VKKLLFAIPL	VPSANPPPLS	МАННННН	368
115 15.7E	VKKLLFAIPL	YLIKPPEGFS	МАННННН	369
116 YJ3.42	VKKLLFAIPL	ISTLHFRAFG	МАННННН	370
117 YJ3.37	VKKLLFAIPL	VRVMCGHSYA	МАННННН	371
118 YJ3.67	VKKLLFAIPL	VLSLSRTFSG	МАННННН	372
119 YJ3.75	VKKLLFAIPL	WCALSRQSMP	МАННННН	373
120 YJ3.86	VKKLLFAIPL	YFWSLRVSWP	МАННННН	374
121 YJ3.33	VKKLLFAIPL	YILSPRLPPP	МАННННН	375
122 YJ3.22	VKKLLFAIPL	VVAAHRFSYA	МАНННННН	376
123 YJ3.62	VKKLLFAIPL	YVHLTSKAIP	МАННННН	377
124 YJ3.59	VKKLLFAIPL	SLTLYRSGWS	МАНННННН	378
125 YJ3.18	VKKLLFAIPL	YYALSGRPVT	МАНННННН	379
126 YJ3.79	VKKLLFAIPL	MLSLMRQSAP	манннннн	380

TABLE 4

Pr	eference s	equence patterns	selected from	L4 S5	sc-dsFv library
No.	Code		Sequence		SEQ ID NO
	M13-pelB	VKKLLFAIPLVVPFY	ААОРАМАННН	ннн	4
1	1.11A	VKKLLFAIPLVVPFY	ARPLTRIQTP	ннн *	381
2	9.3D	VKKLLFAIPLVVPFY	LTQLSRREPS	ннн *	382
3	1.6B	VKKLLFAIPLVVPFY	ARSLATSPSR	ннн *	383
4	14.5H	VKKLLFAIPLVVPFY	PARSYMLVRP	ннн *	384
5	12.2A	VKKLLFAIPLVVPFY	SRSYMLLSRP	ннн *	385
6	12.6H	VKKLLFAIPLVVPFY	TRSALAFFLP	ннн *	386
7	YJ4.13	VKKLLFAIPLVVPFY	SRGFTLPRLI	ннн *	387
8	YJ4.1	VKKLLFAIPLVVPFY	SSAFTRPIRP	ннн *	388
9	12.2E	VKKLLFAIPLVVPFY	TRYSHAFMLI	ннн *	389
10	6.10B	VKKLLFAIPLVVPFY	ARPMSMFRSD	ннн *	390
11	8.4D	VKKLLFAIPLVVPFY	ASSMSqYRQN	ннн *	391
12	5.9H	VKKLLFAIPLVVPFY	ARSYSRPPSI	ннн *	392
13	10.8A	VKKLLFAIPLVVPFY	ASSMSRLRPH	ннн *	393

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TABLE 4 -continued

		TABLE 4	-continue	a	
Pr	eference	sequence patterns	selected from	L4 S5	sc-dsFv library
No.	Code		Sequence		SEQ ID NO
14	YJ4.3	VKKLLFAIPLVVPFY	CRSLSRPMLV	ннн *	394
15	4.6C	VKKLLFAIPLVVPFY	SRSMSLHPTA	ннн *	395
16	CM11	VKKLLFAIPLVVPFY	TRSMTRLAPP	ннн *	396
17	9.8H	VKKLLFAIPLVVPFY	TRAMSVSHKT	ннн *	397
18	13.1F	VKKLLFAIPLVVPFY	LLAPKPSVKR	ннн *	398
19	9.7A	VKKLLFAIPLVVPFY	SRPAPALSRL	ннн *	399
20	15.9C	VKKLLFAIPLVVPFY	AKAMSARYQS	ннн *	400
21	CM18	VKKLLFAIPLVVPFY	FASQRSSPIR	ннн *	401
22	CM24	VKKLLFAIPLVVPFY	CLSFTSARFq	ннн *	402
23	12.1A	VKKLLFAIPLVVPFY	PSASSRLSPK	ннн *	403
24	2.10G	VKKLLFAIPLVVPFY	ARSYTRVPLA	ннн *	404
25	CM2	VKKLLFAIPLVVPFY	ARSLTFLPPR	ннн *	405
26	9.4C	VKKLLFAIPLVVPFY	TTRVNAFMLV	ннн *	406
27	11.11H	VKKLLFAIPLVVPFY	QAFRPVPVRN	ннн *	407
28	11.8H	VKKLLFAIPLVVPFY	TSGMSRLRSW	ннн *	408
29	1.12C	VKKLLFAIPLVVPFY	SRSPSQLSSR	ннн *	409
30	16.12H	VKKLLFAIPLVVPFY	AFSLSRTSSK	ннн *	410
31	3.11F	VKKLLFAIPLVVPFY	FHRVQQFSPA	ннн *	411
32	9.2B	VKKLLFAIPLVVPFY	LDSMLTFRRS	ннн *	412
33	CM40	VKKLLFAIPLVVPFY	CRSLTSPLRM	ннн *	413
34	15.5B	VKKLLFAIPLVVPFY	SRSASFLRPI	ннн *	414
35	9.2F	VKKLLFAIPLVVPFY	MTFqSNSPRG	ннн *	415
36	CM38	VKKLLFAIPLVVPFY	CRPMTLRqPV	ннн *	416
37	CM5	VKKLLFAIPLVVPFY	VRPMSRVIMS	ннн *	417
38	CM36	VKKLLFAIPLVVPFY	SYGFSRPFSK	ннн *	418
39	11.9G	VKKLLFAIPLVVPFY	TRSCFAFMLP	ннн *	419
40	6.8B	VKKLLFAIPLVVPFY	AFSGAFRQSQ	ннн *	420
41	16.6B	VKKLLFAIPLVVPFY	LRAGSFSAAP	ннн *	421
42	CM22	VKKLLFAIPLVVPFY	SHSMAPPSRR	ннн *	422
43	CM31	VKKLLFAIPLVVPFY	CRSGTFGNIG	ннн *	423
44	11.5F	VKKLLFAIPLVVPFY	ARSMASTPLA	ннн *	424
45	YJ4.2	VKKLLFAIPLVVPFY	VYPLAPRLRD	ннн *	425
46	6.10H	VKKLLFAIPLVVPFY	SLPWRRTPFQ	ннн *	426
47	10.3D	VKKLLFAIPLVVPFY	MRTPPLSqRI	ннн *	427
48	CM28	VKKLLFAIPLVVPFY	ARSLSSYNAV	ннн *	428
49	12.4D	VKKLLFAIPLVVPFY	VHALARKSQF	ннн *	429
50	CM25	VKKLLFAIPLVVPFY	SRSFSSPSIT	ннн	430
51	13.5A	VKKLLFAIPLVVPFY	CRALSKPLPP	НМН	431

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TABLE 4 -continued

			1 -continue		
		sequence patterns		L4 S5	
No.	Code		Sequence		SEQ ID NO
52	12.6C	VKKLLFAIPLVVPFY	CRPSAPKMLL	ннн	432
53	CM16	VKKLLFAIPLVVPFY	SRSMSYFqPL	ннн	433
54	4.2C	VKKLLFAIPLVVPFY	TRSLSRSIPH	ннн	434
55	16.6C	VKKLLFAIPLVVPFY	SQLHqSPGNP	ннн	435
56	10.10A	VKKLLFAIPLVVPFY	TRAIARPPYT	ннн	436
57	10.11G	VKKLLFAIPLVVPFY	ARSLSTVRFP	ннн	437
58	CM8	VKKLLFAIPLVVPFY	TRAFSSPLSN	ннн	438
59	9.6D	VKKLLFAIPLVVPFY	NRTPTIqRDS	ннн	439
60	8.4B	VKKLLFAIPLVVPFY	ARAVSRTVPT	ннн	440
61	8.5E	VKKLLFAIPLVVPFY	AqSMAVPIST	ннн	441
62	13.2C	VKKLLFAIPLVVPFY	PqPSRGFMLI	ннн	442
63	CM10	VKKLLFAIPLVVPFY	TRSMVFPAKV	ннн	443
64	CM26	VKKLLFAIPLVVPFY	SRSMTLKGPE	ннн	444
65	CM17	VKKLLFAIPLVVPFY	AFPFSRQPNA	ннн	445
66	CM7	VKKLLFAIPLVVPFY	SRALTSISGM	ннн	446
67	CM6	VKKLLFAIPLVVPFY	CRGMSLNVTR	ннн	447
68	6.10C	VKKLLFAIPLVVPFY	SHWRTQRPPE	ннн	448
69	CM45	VKKLLFAIPLVVPFY	ARSFSSPPGP	ннн	449
70	13.1G	VKKLLFAIPLVVPFY	IFPIEASARR	ннн	450
71	CM39	VKKLLFAIPLVVPFY	ASSMALRPRV	ннн	451
72	YJ4.74	VKKLLFAIPLVVPFY	SRAFSSTPAM	ННН	452
73	1.7F	VKKLLFAIPLVVPFY	SRSMVLQGPT	ннн	453
74	YJ4.28	VKKLLFAIPLVVPFY	SRSMTSPPYI	ннн	454
75	10.3B	VKKLLFAIPLVVPFY	ANRPQSTKNI	ННН	455
76	YJ4.56	VKKLLFAIPLVVPFY	SRALTMTPSF	ннн	456
77	4.6H	VKKLLFAIPLVVPFY	PTRLFAFMLT	ННН	457
78	14.12A	VKKLLFAIPLVVPFY	SRAMSPIPRQ	ННН	458
79	CM29	VKKLLFAIPLVVPFY	ARSMGSMWQL	ннн	459
80	YJ4.42	VKKLLFAIPLVVPFY	SFSMTRSSPL	ннн	460
81	CM42	VKKLLFAIPLVVPFY	SFSFTRqPLP	ннн	461
82	YJ4.33	VKKLLFAIPLVVPFY	NRVPSPASQT	ннн	462
83	YJ4.23	VKKLLFAIPLVVPFY	SFSFSKPRFS	ннн	463
84	CM27	VKKLLFAIPLVVPFY	ARSLTQFSSV	ннн	464
85	YJ4.39	VKKLLFAIPLVVPFY	ARCFSSPVAL	ннн	465
86	11.3B	VKKLLFAIPLVVPFY	GASSWWLFPS	ннн	466
87	YJ4.84	VKKLLFAIPLVVPFY	TPPQQQALLS	ннн	467
88	14.1F	VKKLLFAIPLVVPFY	SRGFSMAFFP	ннн	468
89	CM33	VKKLLFAIPLVVPFY	SLAMSRPqAS	ннн	469

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TABLE 4 -continued

Pr	eference s	equence patterns s	elected from	L4 S5 sc-	dsFv library
No.	Code		Sequence		SEQ ID NO
90	13 120	VKKLLFAIPLVVPFY	TYALTTFqSV	עטט	470
		VKKLLFAIPLVVPFY	-		471
		VKKLLFAIPLVVPFY			472
		VKKLLFAIPLVVPFY	TSALARSPRV		473
	4.8E	VKKLLFAIPLVVPFY			474
	4.0E	VKKLLFAIPLVVPFY			475
	9.2D				
		VKKLLFAIPLVVPFY	FPLSSRAFML		476
		VKKLLFAIPLVVPFY			477
	9.6H	VKKLLFAIPLVVPFY			478
	CM3 7	VKKLLFAIPLVVPFY	SRSMSLSSDL		479
		VKKLLFAIPLVVPFY			480
101	12.1B	VKKLLFAIPLVVPFY	TSCRAMTLPR	ННН	481
102	CM23	VKKLLFAIPLVVPFY	TYPFSRAGPP	ННН	482
103	YJ4.47	VKKLLFAIPLVVPFY	ANQQALPFQL	ннн	483
104	YJ4.38	VKKLLFAIPLVVPFY	GWSMSLRSHS	ннн	484
105	4.11H	VKKLLFAIPLVVPFY	SPQVVTRKDL	ннн	485
106	12.9G	VKKLLFAIPLVVPFY	LRNAHAMASA	ннн	486
107	CM44	VKKLLFAIPLVVPFY	SRSGSFNVTP	ннн	487
108	11.3E	VKKLLFAIPLVVPFY	SRPLSRVPVF	ннн	488
109	11.9F	VKKLLFAIPLVVPFY	SKRMPPPISq	ннн	489
110	CM34	VKKLLFAIPLVVPFY	TRSMSSLPSP	ннн	490
111	14.11DV	KKLLFAIPLVVPFY	CRSSSSIFPL	ннн	491
112	CM15	VKKLLFAIPLVVPFY	RSAHAMSIQT	ннн	492
113	10.1H	VKKLLFAIPLVVPFY	GYCFSARIIR	ннн	493
114	9.10A	VKKLLFAIPLVVPFY	PHLSPLqPQq	ннн	494
115	CM43	VKKLLFAIPLVVPFY	SFSFSRFPGL	ннн	495
116	YJ4.48	VKKLLFAIPLVVPFY	SSSMSLRPQF	ннн	496
117	11.11DV	KKLLFAIPLVVPFY	SSPRARPVPP	ннн	497
118	CM46	VKKLLFAIPLVVPFY	ARSLSALSPY	ннн	498
119	12.5C	VKKLLFAIPLVVPFY	PVRqLHTNLR	ннн	499
120	10.2F	VKKLLFAIPLVVPFY	PITSTPYqSP	ннн	500
121	CM21	VKKLLFAIPLVVPFY	VNALTFLPSq	ннн	501
122	CM41	VKKLLFAIPLVVPFY	ARSLSSPLTL	ННН	502
123	YJ4.25	VKKLLFAIPLVVPFY	TRPPTVGLRQ	ннн	503
124	CM14	VKKLLFAIPLVVPFY	TRALSPMSWq	ннн	504
		VKKLLFAIPLVVPFY			505
126		VKKLLFAIPLVVPFY			506
		VKKLLFAIPLVVPFY			507
14/	101.0/	VARIDDEFITUVVFFI	ZALDLULTOK		507

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TABLE 4 -continued

	TABLE 4	l -continue	ed .	
Preference	sequence patterns	selected from	L4 S5	sc-dsFv library
No. Code		Sequence		SEQ ID NO
128 CM32	VKKLLFAIPLVVPFY	SKAFSSFqAS	ннн	508
129 10.6H	VKKLLFAIPLVVPFY	GYSMSqSGLT	ннн	509
130 YJ4.40	VKKLLFAIPLVVPFY	AQALTTRGLA	ННН	510
131 YJ4.26	VKKLLFAIPLVVPFY	VKSLTRPAFL	ннн	511
132 12.4F	VKKLLFAIPLVVPFY	AqSRLRVYPP	ННН	512
133 4.5B	VKKLLFAIPLVVPFY	PAIGFMLLRY	ннн	513
134 12.3D	VKKLLFAIPLVVPFY	SFGTLVRPRP	ННН	514
135 CM3	VKKLLFAIPLVVPFY	IRRPVDPVMP	ннн	515
136 YJ4.19	VKKLLFAIPLVVPFY	FPLRQTHRYP	ннн	516
137 13.2H	VKKLLFAIPLVVPFY	THSMQRPTGR	ннн	517
138 10.5D	VKKLLFAIPLVVPFY	RHTqLSSSTS	ннн	518
139 15.10D	VKKLLFAIPLVVPFY	SCGFSRLSKA	ннн	519
140 CM35	VKKLLFAIPLVVPFY	SRSFSQLPHI	ннн	520
141 YJ4.43	VKKLLFAIPLVVPFY	SSSMSQLRPF	ннн	521
142 10.2B	VKKLLFAIPLVVPFY	CRTTFALQSS	ннн	522
143 CM19	VKKLLFAIPLVVPFY	AQSMSIRHNN	ннн	523
144 11.4E	VKKLLFAIPLVVPFY	NSRFRTTPPS	ннн	524
145 CM20	VKKLLFAIPLVVPFY	SVSMSRYQLS	ннн	525
146 CM12	VKKLLFAIPLVVPFY	SSGASRLRIL	ННН	526
147 YJ4.81	VKKLLFAIPLVVPFY	CWSLSRPRLL	ннн	527
148 10.1C	VKKLLFAIPLVVPFY	TSRSTKLTPS	ннн	528
149 11.6D	VKKLLFAIPLVVPFY	SRVSVAFMLM	ннн	529
150 YJ4.72	VKKLLFAIPLVVPFY	CLGRSMAPGP	ннн	530
151 14.1A	VKKLLFAIPLVVPFY	FVHRRDSSSL	ННН	531
152 YJ4.24	VKKLLFAIPLVVPFY	SLGFSRLTSL	ннн	532
153 13.2B	VKKLLFAIPLVVPFY	ASALSRRVPq	ннн	533
154 11.6B	VKKLLFAIPLVVPFY	TYPASWPRLR	ннн	534
155 9.2G	VKKLLFAIPLVVPFY	SRVSLAVTPS	ннн	535
156 10.11B	VKKLLFAIPLVVPFY	NNPFSSISqq	ннн	536
157 11.8D	VKKLLFAIPLVVPFY	RPLPRPFAGN	ннн	537
158 CM4	VKKLLFAIPLVVPFY	GFSMTQYLPq	ннн	538
159 YJ4.75	VKKLLFAIPLVVPFY	SSALSRSFYP	ннн	539
160 YJ4.61	VKKLLFAIPLVVPFY	TQQRCFAMHI	ннн	540
161 YJ4.85	VKKLLFAIPLVVPFY	IKHFYNSRPS	ннн	541
162 YJ4.51	VKKLLFAIPLVVPFY	FTRLPKESSP	ННН	542
163 9.6G	VKKLLFAIPLVVPFY	LPAQPRVTRT	ннн	543
164 CM13	VKKLLFAIPLVVPFY	LRSMTLNTST	ННН	544
165 YJ4.35	VKKLLFAIPLVVPFY	PDTFSYSSQD	ннн	545

TABLE 4 -continued

Prefere	ence sequence patterns	selected from	L4 S5	sc-dsFv library
No. Code	•	Sequence		SEQ ID NO
166 YJ4.	.41 VKKLLFAIPLVVPFY	FRNPQLPSSA	ннн	546
167 YJ4.	.50 VKKLLFAIPLVVPFY			547
168 9.80	VKKLLFAIPLVVPFY	qSHTILPLPA	ннн	548
169 CM9	VKKLLFAIPLVVPFY	SSAFqPMVSS	ннн	549
170 9.7F	H VKKLLFAIPLVVPFY	QSRRLPILPL	ннн	550
171 YJ4.	31 VKKLLFAIPLVVPFY	GQAYLPAPQL	ннн	551
172 9.11	LB VKKLLFAIPLVVPFY	TSRPRETLFL	ннн	552
173 9.30	3 VKKLLFAIPLVVPFY	TAASVVRSRD	ннн	553
174 10.5	F VKKLLFAIPLVVPFY	VRGAAPKFSV	ннн	554
175 YJ4.	.14 VKKLLFAIPLVVPFY	FRHQPASVST	ннн	555
176 9.8E	3 VKKLLFAIPLVVPFY	PTNAIAFFLq	ннн	556
177 YJ4.	.59 VKKLLFAIPLVVPFY	LKSLRSDTPN	ннн	557
178 YJ4	.22 VKKLLFAIPLVVPFY	IKRPLPLAPT	ннн	558
179 11.1	L1F VKKLLFAIPLVVPFY	ASSSKSRFML	ннн	559
180 YJ4.	82 VKKLLFAIPLVVPFY	PWKPRLLPPQ	ннн	560
181 9.1F	H VKKLLFAIPLVVPFY	SRGFMLTLRY	ннн	561
182 9.8E	VKKLLFAIPLVVPFY	CKARGIMPVF	ннн	562
183 YJ4.	.17 VKKLLFAIPLVVPFY	ASLPRLTSQS	ннн	563
184 11.2	B VKKLLFAIPLVVPFY	qSSAFSYMLS	ннн	564
185 10.7	7A VKKLLFAIPLVVPFY	SFSSQRFLRP	ннн	565
186 9.70	VKKLLFAIPLVVPFY	TSSNTSRRFP	ннн	566
187 11.1	LOB VKKLLFAIPLVVPFY	NqTAATAPPR	ннн	567
188 10.8	G VKKLLFAIPLVVPFY	GAPLSWRRSY	ннн	568
189 9.10	DD VKKLLFAIPLVVPFY	CRSVWCIPRP	ннн	569
190 9.10	VKKLLFAIPLVVPFY	AKACLRPLQT	ннн	570
191 9.6E	VKKLLFAIPLVVPFY	CLASSHRHRP	ннн	571
192 11.3	H VKKLLFAIPLVVPFY	LRADSLAPKS	ннн	572
193 9.9E	7 VKKLLFAIPLVVPFY	SVPQFSGRSR	ннн	573
194 YJ4.	78 VKKLLFAIPLVVPFY	VYPARFPAKT	ннн	574
195 YJ4.	21 VKKLLFAIPLVVPFY	NFMLRHPQTF	ннн	575
196 YJ4.	32 VKKLLFAIPLVVPFY	YVPRFPPKSA	ннн	576
197 YJ4.	86 VKKLLFAIPLVVPFY	LSPMSRTRYV	ннн	577
198 YJ4.	66 VKKLLFAIPLVVPFY	TYPLTKPYRP	ннн	578
199 YJ4	83 VKKLLFAIPLVVPFY	SSYWSHRKPP	ннн	579
200 10.8	C VKKLLFAIPLVVPFY	SPRTFAFFLM	ннн	580
201 11.1	LA VKKLLFAIPLVVPFY	LGPGIRKKPA	ннн	581
202 9.41	VKKLLFAIPLVVPFY	TRLCVAKVAG	ннн	582
203 11.2	E VKKLLFAIPLVVPFY	RSLPASGASR	ннн	583

TABLE 4 -continued

Pr	eference	sequence patterns	selected from	L4 S5	sc-dsFv library
No.	Code		Sequence		SEQ ID NO
204	10.5E	VKKLLFAIPLVVPFY	ASPRVKSYSP	HHH	584
205	9.10F	VKKLLFAIPLVVPFY	PSRTFAFYLV	ннн	585
206	9.4H	VKKLLFAIPLVVPFY	qqЕFАМАННН	ннн	586
207	11.8B	VKKLLFAIPLVVPFY	PqSSKAFFLN	ннн	587
208	11.2F	VKKLLFAIPLVVPFY	VKALRGSYPT	ннн	588
209	11.7F	VKKLLFAIPLVVPFY	TqPSqVRYML	ннн	589
210	11.9C	VKKLLFAIPLVVPFY	SARGqHVRPP	ннн	590
211	10.11C	VKKLLFAIPLVVPFY	STRCPGFFLq	ннн	591
212	11.6E	VKKLLFAIPLVVPFY	CPSVFSRTPP	ннн	592
213	11.3A	VKKLLFAIPLVVPFY	DASSWRHFLS	ннн	593

Example 4

Production of sc-dsFv against H5 of Influenza Virus and Microarray Test

As described above, scFvs (8a and 12a) and their disulfide forms (ds-8a and ds-12a, respectively) to various hemagglutins (HAs) from different serotypes of influenza virus were developed. As shown in FIG. 5, the results indicated that selected scFv phage clones against H5 of influenza virus could be introduced to sc-dsFv directly but had lower binding affinity as compared with original scFvs. These results also suggested that the binding affinity could be enhanced by sc-dsFv phage panning procedures with the signal sequences described above.

The 8aS5 protein could be concentrated to 6 mg/ml without 40 precipitation. The array studies suggested that 4 ng/spot of ds-8a protein could detect ~10⁷ viruses in solution by using 40 nm fluorescence beads. In conclusion, the signal sequence derived from sc-dsFv phage production against VEGF from monoclonal antibody could be applied for sc-dsFv phage 45 production against hemagglutinin from natural antibody repertoire. The binding affinity could be enhanced by sc-dsFv phage panning procedures to produce sc-dsFv with high binding capacity and better stability than scFv for further applications.

Example 5

Soluble Non-fusion sc-dsFv Expressed with Suppressor *E. coli* Strain

The signal sequences resulting in the successful expression of the displayed sc-dsFv on phage rescued from suppressor *E. coli* strain ER2738 were more likely to result in secretion of the soluble non-fusion anti-VEGF sc-dsFv in a culture 60 medium. Signal sequence phage library L4 was selected for binding to immobilized VEGF and the VEGF-binding enriched phage variants were amplified for the next round of selection/amplification cycle. The selection/amplification cycle was repeated for four rounds. After each round of selection/amplification cycle, a random collection of 96 phage variants were picked from the amplified phage population.

These phage variants were used to infect *E. coli* ER2738 and the soluble sc-dsFv was expressed in the overnight cultures, which were tested for binding to immobilized VEGF with ELISA.

These random collections of phage variants were also used to infect *E. coli* HB2151 for the same assay to determine the sc-dsFv secretion. The result showed that, with ER2738 as the host, 0%, 0%, 2%, and 14% of the phage variants from 1st, 2nd, 3rd, and 4th round of selection/amplification cycle respectively secreted functional sc-dsFv binding to VEGF with ELISA signal greater than OD_{450 nm}>0.6. But this trend was not found in the experiment with *E. coli* strain HB2151. This result indicated that signal sequence alteration could restore the secretion of the soluble non-fusion sc-dsFv and that the search for the optimum signal sequences could be facilitated with phage-based selection/amplification cycles on signal sequence libraries. This conclusion is applicable only to the *E. coli* suppressor strain ER2738 as the bacteria host for the M13 phage.

Example 6

Interface Disulfide Bond Formation in the sc-dsFv

One measurement for the folding quality of the sc-dsFv is the extent of the interface disulfide bond formation in the sc-dsFv. This measurement was determined by the ratio of the sc-dsFv-VEGF binding ELISA signal after the fXa (bovine factor Xa) treatment over that before the fXa treatment. FXa cleaves substrate sequence -IEGR- in the linker peptide connecting the two variable domains in the sc-dsFv construct. If the interface disulfide bond was not formed in the sc-dsFv, the cleavage of the linker peptide would result in dissociation of the variable domains and abolishment of the affinity against VEGF. Hence the ratio reflects the percentage of interface disulfide bond formation in the sc-dsFv. This measurement was validated with the positive control (anti-VEGF scFv (fXa+)/M13pIII-pelB with -IEGR- (SEQ ID NO:599) in the

linker peptide but without the interface disulfide bond) and the negative control (anti-VEGF scFv(fXa-)/M13pIII-pelB without both the fXa cutting site and the interface disulfide bond).

FIG. 6A compared the extent of the interface disulfide bond formation in the secreted soluble sc-dsFv with the disulfide bond formation in the sc-dsFv displayed on phage surface for the signal sequence variants from the L4 library. Strong correlation between the two measurement is evident (R²=0.508, p-value=0.000158). As shown in FIG. 6A, signal sequence optimization could improve the disulfide bond formation in the sc-dsFv from ~0% up to 40% of the secreted sc-dsFv molecule.

Another folding quality of the sc-dsFv was determined by the ratio of the normalized sc-dsFv-VEGF binding ELISA signal over the normalized quantity of the secreted sc-dsFv determined by electrophoresis and Western blot analysis. FIG. 6B compared the extent of the interface disulfide bond formation in the secreted soluble sc-dsFv with the folding qualities derived from electrophoresis and ELISA measurements for the signal sequence variants from the L4 library. The positive correlation ($R^2=0.296$, p-value=0.062) shown in FIG. 6B indicated that the interface disulfide bond formation 25 enhanced the affinity for the sc-dsFv-VEGF interaction. The plot also indicated that the selected variants resulted in secreted sc-dsFv with up to more than 10-fold VEGF-binding signals per unit quantity of secreted sc-dsFv compared with the positive control scFv(fXa+)/M13pIII-pelB, indicating 30 that the secreted sc-dsFv from these signal sequence variants folded into antibody-like structure substantially more effectively that the scFv construct. This is most likely due to the stabilizing interface disulfide bond that is formed in the scdsFv but is absent in the scFv construct.

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Example 7

Correlation between the Stability of sc-dsFv and the Extent of the Interface Disulfide Bond Formation in the sc-dsFv

The effect of interface disulfide bond in stabilizing the sc-dsFv structure was demonstrated in FIG. 7. Secreted scdsFv from representative variants selected from each of the three libraries were expressed and incubated at 37° C. for 12 days and the affinities of the sc-dsFv's against VEGF were measured along the course of incubation. FIG. 7A shows the VEGF-binding affinity plotted against the time course of incubation for each of the selected variants. The VEGF affinity for the control anti-VEGF scFv dropped rapidly in the first few days of incubation, while a few variants from L4 library resulted in stable secreted sc-dsFv that were even gaining affinities against VEGF compared with freshly prepared secreted protein, presumably due to the increasingly stabilized sc-dsFv with the formation of the interface disulfide bond. The correlation between the two measurements shown in FIG. 7B is strong (R²=0.867 p-value=0.023), indicating that the interface disulfide bond could be one of the most important factors in stabilizing the secreted sc-dsFv in the culture medium.

All of the features disclosed in this specification may be combined in any combination. Each feature disclosed in this specification may be replaced by an alternative feature serving the same, equivalent, or similar purpose. Thus, unless expressly stated otherwise, each feature disclosed is only an example of a generic series of equivalent or similar features. From the above description, one skilled in the art can easily ascertain the essential characteristics of the present invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions. Thus, other embodiments are also within the scope of the following claims.

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<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 51
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Val Lys Lys Leu Leu Trp His Val Leu Pro Tyr Leu Pro Asn Ser Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
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<220> FEATURE:
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<400> SEQUENCE: 52
Val Lys Lys Leu Leu Ser Ile Val Pro Leu Phe Ser Pro Gln Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
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<213> ORGANISM: artificial
<220> FEATURE:
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Val Lys Lys Leu Leu Val Met Thr Ser Pro Met Leu Ala Pro Gly Ala
Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 54
Val Lys Lys Leu Leu Val Leu Ser Leu Pro Ser Ile Ala Pro His Ala
Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 55
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Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
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<220> FEATURE:
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<400> SEQUENCE: 56
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Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
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<220> FEATURE:
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<400> SEQUENCE: 57
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Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEOUENCE: 58
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 59
Val Lys Lys Leu Leu Leu Ala Ser Trp Leu Phe Arg Ala Asp Met Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
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Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
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<220> FEATURE:
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Ala Gln Pro Ala Met Ala His His His His His
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Ala Gln Pro Ala Met Ala His His His His His
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<220> FEATURE:
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<400> SEQUENCE: 63
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 64
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 64
Val Lys Lys Leu Leu Leu Met Pro Phe Leu Asn Gln Ser Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 65
Val Lys Lys Leu Leu Phe Thr Ser Gly Leu Lys Leu Val Pro Pro Ala
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                                   10
Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 67
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Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
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<220> FEATURE:
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<400> SEQUENCE: 68
Val Lys Lys Leu Leu Leu Gly Gln Ser Leu Met His Phe Gln Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 69
Val Lys Lys Leu Leu Pro Gln Leu Ala Met Ser Leu Pro Ser Ile Ala
     5
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 70
Val Lys Lys Leu Leu Tyr Glu Thr Met Leu Ser Ser Tyr Leu Tyr Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 71
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Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 72
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 73
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Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 74
Val Lys Lys Leu Leu Leu Leu Thr Leu Met Gln Pro Thr Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 75
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 75
Val Lys Lys Leu Leu Phe Asp Phe Phe Thr His Val His Leu Phe Ala
                          10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 76
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 76
Val Lys Lys Leu Leu Ala Leu Tyr Pro His Phe Val Ser Phe Thr Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 77
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 77
Val Lys Lys Leu Leu Pro Tyr Ala Ile Gln Leu Phe Ser Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 78
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 78
Val Lys Lys Leu Leu Trp Phe Pro Leu His Ser Ser Leu Leu Pro Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 79
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 79
Val Lys Lys Leu Leu Pro Ala Leu Leu Leu Ala Thr Ala Ala Phe Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 80
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 80
Val Lys Lys Leu Leu Leu Ala Ser Val Ala Trp Asn Leu Asp Ser Ala
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Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 81
<211> LENGTH: 28
<212> TYPE: PRT
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 82
Val Lys Lys Leu Leu Ser Pro Leu Leu Phe Leu Gln Asn Tyr Thr Ala
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                       10
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 83
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 84
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 84
Val Lys Lys Leu Leu Val Pro Ser Phe Leu Leu Ser Pro Ser Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 85
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 85
Val Lys Lys Leu Leu Ser Leu Tyr Trp Leu Thr Ser Gln Pro Leu Ala
            5
                                10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 86
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<211> LENGTH: 28

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<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 86
Val Lys Lys Leu Leu Phe Ala Leu Ser Ser Val His Ser Pro Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 87
Val Lys Lys Leu Leu Ser Tyr Tyr Ser Leu Leu Tyr Ser Tyr Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 88
Val Lys Lys Leu Leu Leu Val Ser Gly Leu Gln Pro Trp Tyr Phe Ala
1
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 89
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 89
Val Lys Lys Leu Leu Val Leu Ala Thr Pro Leu His Leu Ser Pro Ala
1
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 90
Val Lys Lys Leu Leu Ser Leu Ala Phe Pro Leu Phe Thr Pro Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 91
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 92
Val Lys Lys Leu Leu Gln Pro Val Leu Phe Ser Phe Phe Ile Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 93
Val Lys Lys Leu Leu Met Ser Gln Phe Leu Asn Leu Leu Ser Pro Ala
                                   10
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 94
Val Lys Lys Leu Leu Trp Ala Val Gln Pro Leu Phe Pro Leu Asn Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 95
Val Lys Lys Leu Leu Met Phe Ser Leu Val Pro Ser Pro Pro Ile Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 96
Val Lys Lys Leu Leu Pro Phe Phe Leu Gln Pro Phe Gln Phe Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 97
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEO ID NO 98
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 98
Val Lys Lys Leu Leu Phe Trp Gln Phe Leu Trp Pro Ser Leu Pro Ala
                                   10
Ala Gln Pro Ala Met Ala His His His His His
           2.0
<210> SEQ ID NO 99
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 99
Val Lys Lys Leu Leu Leu Gly Gln Phe Phe Pro Asn Pro Met Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 100
Val Lys Lys Leu Leu Thr Leu Ser Ala Leu Ser Gln Trp His Pro Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 101
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 102
Val Lys Lys Leu Leu Phe Ala Phe Ala Pro Ala Pro Phe Tyr His Ala
                                 10
Ala Gln Pro Ala Met Ala His His His His His
          20
                              25
<210> SEQ ID NO 103
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 103
Val Lys Lys Leu Leu Phe Leu Pro Phe Ala Leu Val Pro Arg Gln Ala
1 5
                      10
Ala Gln Pro Ala Met Ala His His His His His
          20
                              25
<210> SEQ ID NO 104
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 104
Val Lys Lys Leu Leu Ala Leu Trp Met Gln Leu Tyr Pro Gln Asp Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 105
Val Lys Lys Leu Leu Ala Ser Ile Leu Phe Ser His Ala Ala Pro Ala
                                  10
Ala Gln Pro Ala Met Ala His His His His His
        20
                     25
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 106
Val Lys Lys Leu Leu Leu Pro Leu Pro Trp Ser Leu His Leu Tyr Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 107
Val Lys Lys Leu Leu Pro His Phe Met Ser Phe Trp Phe Glu Ala
                                   10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 108
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 108
Val Lys Lys Leu Leu Leu Phe Gln Pro Phe Trp Pro Ile Pro Tyr Ala
                                   10
Ala Gln Pro Ala Met Ala His His His His His
          20
<210> SEQ ID NO 109
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 109
Val Lys Lys Leu Leu Leu Phe Ser Leu Gly Arg Leu Pro Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 110
Val Lys Lys Leu Leu Pro Leu Trp Val Leu Leu Lys Asp Pro Leu Ala
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Ala Gln Pro Ala Met Ala His His His His His

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20
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<210> SEQ ID NO 111
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 111
Val Lys Lys Leu Leu Met Ser Phe Ala Thr Leu Phe Pro His Asn Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 112
Val Lys Lys Leu Leu Gln His Ser Leu Val Thr Ser Trp Leu Cys Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 113
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 113
Val Lys Lys Leu Leu Leu Phe Gln Gly Ala Phe Val Gly Gln Ala
             5
Ala Gln Pro Ala Met Ala His His His His His
          20
<210> SEQ ID NO 114
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 114
Val Lys Lys Leu Leu Trp Met Phe His Ser Leu Pro Phe Ser Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 115
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 115
Val Lys Lys Leu Leu Leu Thr Gln Leu Leu Leu Thr Arg Leu His Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 116
Val Lys Lys Leu Leu Ala Leu Thr Leu Val Pro Ser Ser Tyr Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 117
Val Lys Lys Leu Leu Leu Pro Trp Tyr Met Leu Leu Ser Asp Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
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<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 118
Val Lys Lys Leu Leu Val Val Thr Gln Phe Trp Pro Ser Leu Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 119
Val Lys Lys Leu Leu Leu Ser Thr Leu Phe Leu Trp His Val Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 120
Val Lys Lys Leu Leu Arg Ser Leu Phe Phe Gln Gln Leu Tyr Pro Ala
1 5
                         10
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Ala Gln Pro Ala Met Ala His His His His His
           20
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 121
Val Lys Lys Leu Leu Thr Leu Thr Thr Leu His Gln Thr Phe Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 122
Val Lys Lys Leu Leu Ser Ala Leu Leu Ala Pro Trp Tyr Trp Asp Ala
                                   10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 123
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 123
Val Lys Lys Leu Leu Ala Ile Gln Gln Arg Met Gln Ile Tyr Thr Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 124
Val Lys Lys Leu Leu Leu Phe Pro Trp Phe Gln Pro Pro Tyr Ala
Ala Gln Pro Ala Met Ala His His His His His
           2.0
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<210> SEQ ID NO 125
<211 > LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 125
Val Lys Lys Leu Leu Tyr Phe Thr Ser Leu Leu Gly Gln Phe Pro Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 126
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 126
Val Lys Lys Leu Leu Pro Val Leu Ile Phe Leu Ser Glu Ile Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 127
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 127
Val Lys Lys Leu Leu Val Ala Thr Ser Leu Arg Trp Ala Val Thr Ala
1
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 128
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 128
Val Lys Lys Leu Leu Ala Gln Leu Phe His Leu Phe Ala Thr His Ala
1
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 129
Val Lys Lys Leu Leu Gln Phe Ser Ala Leu Phe Asn Ser Phe Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 130
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 130
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Val Lys Lys Leu Leu Phe His Leu Met Ser Met Leu Pro Pro Pro Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 131
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 131
Val Lys Lys Leu Leu Pro Val Cys Ser Gln Ser Met Phe Pro Ile Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 132
Val Lys Lys Leu Leu Leu Leu Ser Ser Ser Tyr Gln Ser Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
           2.0
<210> SEQ ID NO 133
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 133
Val Lys Lys Leu Leu Leu Asp Ser Leu Phe Phe His Ala Pro Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 134
Val Lys Lys Leu Leu Gln Ala Trp Val Phe Ser Ala His Gln Leu Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 135
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Val Lys Lys Leu Leu Phe Gln Ala Leu Gly Ala Leu Thr Ser Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 136
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 136
Val Lys Lys Leu Leu Cys Phe Phe Phe Phe Leu Gln Phe His Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 137
Val Lys Lys Leu Ceys Phe Ser His Leu Ala Leu Pro Ser Pro Ala
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Ala Gln Pro Ala Met Ala His His His His His
           2.0
<210> SEQ ID NO 138
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 138
Val Lys Lys Leu Leu Phe Gly Ser Trp Ile Pro Phe Thr Gln Met Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 139
Val Lys Lys Leu Leu Gly Leu Gly Tyr Phe Asn Trp Thr Leu Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
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Val Lys Lys Leu Leu His Leu Phe Pro Leu Phe Gln Phe His His Ala
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1
        5
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 141
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 141
Val Lys Lys Leu Leu Ser Glu His Val Ser Ser Ile Cys Val Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 142
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 142
Val Lys Lys Leu Leu Phe Ser Cys Leu Leu Asp Pro Thr Cys Pro Ala
                      10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 143
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 143
Val Lys Lys Leu Leu Leu Tyr Leu Leu His Pro Ser Phe Leu Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 144
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 144
Val Lys Lys Leu Leu Trp Cys Ala Pro Leu Leu Tyr Ser Leu Arg Ala
              5
                                  10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 145
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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Val Lys Lys Leu Leu Phe Ala Met Phe Pro Tyr Thr Phe Gln Thr Ala
                                 10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 146
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 146
Val Lys Lys Leu Leu Pro Ser Leu Phe Tyr Val Glu Ser Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 147
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 147
Val Lys Lys Leu Leu Ser Leu Trp Leu Ser Ser Leu Ser Val Leu Ala
                                  10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 148
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 148
Val Lys Lys Leu Leu Pro His Leu Trp Phe Leu Trp Ser Leu Lys Ala
     5
                                  10
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 149
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 149
Val Lys Lys Leu Leu Ala Ser Asp Pro Val Trp Tyr Phe Leu Trp Ala
Ala Gln Pro Ala Met Ala His His His His His
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                              25
<210> SEQ ID NO 150
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 150
Val Lys Lys Leu Gly Leu Pro Leu Met Gly Leu Gln Ser Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 151
Val Lys Lys Leu Leu Pro Gln Leu Leu Leu Leu Arg Ala Leu Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 152
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 152
Val Lys Lys Leu Leu Ala Pro Ser Ala Phe Ser Leu His Leu Phe Ala
Ala Gln Pro Ala Met Ala His His His His His
           2.0
<210> SEQ ID NO 153
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 153
Val Lys Lys Leu Leu Phe Gln Leu Ser Ser Leu Phe Val Pro Tyr Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 154
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 154
Val Lys Lys Leu Leu Val Pro Ser Phe Leu Ser Thr Met Ile Glu Ala
                      10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 155
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 155
Val Lys Lys Leu Leu Ala Ser Pro Phe Phe Ala Ser Tyr Leu Trp Ala
                                  10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 156
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 156
Val Lys Lys Leu Leu Gln Tyr Leu Leu Ser Pro Ile Gly Tyr Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 157
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 157
Val Lys Lys Leu Leu Val Leu Ser Val Pro Ile Ser Ala His His Ala
                                   10
Ala Gln Pro Ala Met Ala His His His His His
           2.0
<210> SEQ ID NO 158
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 158
Val Lys Lys Leu Leu Met Met Gln Ala Leu Ser Ser Leu Pro Glu Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 159
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 159
Val Lys Lys Leu Leu Met Pro Ala Val Leu Ala Thr Arg Leu Thr Ala
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Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 160
<211> LENGTH: 28
<212> TYPE: PRT
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<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 160
Val Lys Lys Leu Leu Pro Phe Thr Ala Trp Ile Ile Asp Gly Trp Ala
                                  10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 161
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 161
Val Lys Lys Leu Leu Thr Gln Leu Leu Pro Leu Trp Gln Pro Leu Ala
                       10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 162
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 162
Val Lys Lys Leu Leu Leu Val Pro Ser Leu Leu Pro Leu Thr Gln Ala
                                 10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 163
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 163
Val Lys Lys Leu Leu Pro Ile Gln Ser Cys Met Val Ile Pro Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 164
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 164
Val Lys Lys Leu Leu Trp Ser Leu His Leu Ala Thr Arg Leu Leu Ala
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                                 10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 165
<211> LENGTH: 28
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 165
Val Lys Lys Leu Leu Gln Gln Val Leu Leu Cys Ser Thr Leu Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 166
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 166
Val Lys Lys Leu Leu Leu Leu Arg Tyr Phe Leu Asp Pro Met Tyr Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 167
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 167
Val Lys Lys Leu Leu Ile Pro Gln Phe Leu Arg Ser His His Arg Ala
1
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 168
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 168
Val Lys Lys Leu Leu Gly Val Leu His Leu Ala Leu Ser Leu Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 169
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 169
Val Lys Lys Leu Leu Leu Val Thr Ser Gln Phe Ser Leu Val Pro Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 170
Val Lys Lys Leu Leu Pro Leu Ala Leu Ser Trp Phe Gln Leu Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 171
Val Lys Lys Leu Leu Gln His Gln Trp Tyr Pro Thr Val Leu Met Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 172
Val Lys Lys Leu Leu Leu Met Tyr Trp Leu Ser Lys Pro Leu Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 173
Val Lys Lys Leu Leu Thr Gln Leu Thr Leu Ser Ser Pro Ile Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 174
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 174
Val Lys Lys Leu Leu Gln Leu Thr Ala Leu Leu Ser Arg Leu Ile Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 175
Val Lys Lys Leu Leu Leu Met Thr Phe Gly Thr Thr Pro Gln Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 176
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 176
Val Lys Lys Leu Leu Ser Ala Phe Ser Phe Ser Leu Ser Ser Thr Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEO ID NO 177
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 177
Val Lys Lys Leu Leu Ala Pro Trp Leu Val Leu Pro His Phe Pro Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 178
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 178
Val Lys Lys Leu Leu His Val Leu Ser Phe Ala Pro Pro Met Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 179
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 179
Val Lys Lys Leu Leu Asn Trp Leu Phe Phe Ala His Pro Phe Ser Ala
                        10
Ala Gln Pro Ala Met Ala His His His His His
           20
                               25
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<210> SEQ ID NO 180
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 180
Val Lys Lys Leu Leu Gln Leu Ala Val Leu Leu Gly Ser Leu Arg Ala
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Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 181
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 181
Val Lys Lys Leu Leu Leu Phe Gly Leu Phe Tyr Phe Arg Ala Cys Ala
                                 10
Ala Gln Pro Ala Met Ala His His His His His
          20
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<210> SEQ ID NO 182
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 182
Val Lys Lys Leu Leu Phe Gln Phe Phe Val Val Trp Arg Leu Leu Ala
1 5
                      10
Ala Gln Pro Ala Met Ala His His His His His
          20
                              25
<210> SEQ ID NO 183
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 183
Val Lys Lys Leu Leu Pro Trp Ala Trp Pro Pro Pro Pro Phe Trp Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 184
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 184
Val Lys Lys Leu Leu Cln Leu Val Ile Val Tyr Tyr Leu Arg Ala
                                  10
Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 185
Val Lys Lys Leu Leu Arg Gln Ser Val Leu Leu Ser Ala Leu His Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 186
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 186
Val Lys Lys Leu Leu Val Tyr Gly Tyr Phe Leu Thr Thr Phe Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 187
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 187
Val Lys Lys Leu Leu Cys Phe Ser Pro Leu Phe Gly Phe His Thr Ala
                                    10
Ala Gln Pro Ala Met Ala His His His His His
          20
<210> SEQ ID NO 188
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 188
Val Lys Lys Leu Leu Pro Gly Tyr Ala Leu Trp Gln Thr Ile Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 189
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 189
Val Lys Lys Leu Leu Gln Arg Ile Phe Ile Cys Phe Phe Leu Arg Ala
             5
                                   10
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Ala Gln Pro Ala Met Ala His His His His His

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20
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<210> SEQ ID NO 190
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 190
Val Lys Lys Leu Leu Pro His Val Phe Ser Cys Gln Leu Ser Ala Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 191
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 191
Val Lys Lys Leu Leu Ser Pro Leu Ser Leu Ser Val Lys Leu Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 192
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 192
Val Lys Lys Leu Leu Ala Arg Ser Leu Phe Ser Gly Ser Met Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 193
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 193
Val Lys Lys Leu Leu Gln Phe Leu Ile Val Phe Pro Leu Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 194
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 194
Val Lys Lys Leu Leu Leu Ala Val Leu Leu Gly Gln Ser Leu Arg Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 195
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 195
Val Lys Lys Leu Leu Leu Ser His Leu Phe Leu Arg Leu His Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 196
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 196
Val Lys Lys Leu Leu Leu Ala Met Val Phe Phe Val Thr Leu Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 197
Val Lys Lys Leu Leu Trp Leu Phe Ala Leu Pro Gln Glu Asn Val Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 198
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 198
Val Lys Lys Leu Leu His Pro Leu Val Leu Leu Ser Ser Ser Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 199
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 199
Val Lys Lys Leu Leu Gln Tyr Leu Phe Met Leu Ser Met Arg Ala
1 5
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 200
Val Lys Lys Leu Leu Pro Ala Leu Leu Ile Arg Tyr Ala Ser Val Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 201
Val Lys Lys Leu Leu Gln Gln Phe Thr Ser Pro Phe Leu Leu Leu Ala
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Ala Gln Pro Ala Met Ala His His His His His
          2.0
                              25
<210> SEQ ID NO 202
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 202
Val Lys Lys Leu Leu Ser Pro Cys Phe Phe Leu Leu Tyr Leu Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 203
Val Lys Lys Leu Leu Pro Gly Met Pro Leu Phe Phe Thr Asn Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211 > LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 204
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Val Lys Lys Leu Leu Pro Gln Val Phe Phe Leu Phe Arg Pro Phe Ala

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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 205
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 205
Val Lys Lys Leu Leu Pro Phe Pro Ile Leu Leu Gln Ser Pro Phe Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 206
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 206
Val Lys Lys Leu Leu Phe Gln Ala Cys Cys Leu Phe Pro Leu Gln Ala
1
                                   10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 207
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 207
Val Lys Lys Leu Leu Ala Val Val His Thr Met Pro Leu Phe Ser Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 208
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 208
Val Lys Lys Leu Leu Gln Phe Ser Trp Ala Phe Val Ser Ile Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 209
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Val Lys Lys Leu Leu Pro Val Cys Leu Phe Trp Ser Phe Phe Arg Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 210
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 210
Val Lys Lys Leu Leu Gln Leu Leu Trp Gln Gln Gln Val Pro Val Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 211
Val Lys Lys Leu Leu Pro Leu Gln Ala Leu Ser Trp Phe Leu Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
           2.0
<210> SEQ ID NO 212
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 212
Val Lys Lys Leu Leu Phe Tyr Leu Leu Cys Arg Leu Ser Leu Gln Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 213
Val Lys Lys Leu Leu Tyr Leu Gln Ile Leu Val Ile Cys Leu Arg Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 214
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Val Lys Lys Leu Leu Gln Leu Phe Leu Ile Val Phe Pro Leu Arg Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 215
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 215
Val Lys Lys Leu Leu Pro Leu His Phe Ala Leu Phe Phe Arg Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 216
Val Lys Lys Leu Leu Pro Phe Pro Met His Leu Val Leu Pro Phe Ala
                                  10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 217
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 217
Val Lys Lys Leu Leu Pro Leu Leu Phe Ser Pro Pro Ser Leu His Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 218
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 218
Val Lys Lys Leu Cys Gln Ser Ile Thr Phe Ser Ser Ile Trp Ala
                                   10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 219
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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<400> SEQUENCE: 219
Val Lys Lys Leu Leu Trp Gln Arg Leu Phe Pro Phe Leu Leu Ile Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 220
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 220
Val Lys Lys Leu Leu Met Val Pro Phe Trp Pro Phe Ser Phe Thr Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 221
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 221
Val Lys Lys Leu Leu Gln Ala Phe Pro Leu Pro Pro Leu Leu Val Ala
                                10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 222
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 222
Val Lys Lys Leu Leu Pro Leu Tyr Leu Leu Phe Arg Ser Phe Val Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 223
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 223
Val Lys Lys Leu Leu His Arg Ser Met Tyr Leu Ser Trp Leu Tyr Ala
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                                   10
Ala Gln Pro Ala Met Ala His His His His His
           2.0
<210> SEQ ID NO 224
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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Val Lys Lys Leu Leu Leu Ser Thr Leu Val Arg Ala Pro Tyr Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 225
Val Lys Lys Leu Leu Pro Leu Ala Leu Ser Gln Trp Phe Leu Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 226
Val Lys Lys Leu Leu Ala Gln Gly Met Ile Phe Phe Leu Arg Leu Ala
                                  10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 227
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 227
Val Lys Lys Leu Leu Phe Cys Cys Arg Leu Ala Leu Gln Phe Phe Ala
     5
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 228
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 228
Val Lys Lys Leu Leu Tyr Leu Gln Phe Leu Ser Leu Met Leu Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 229
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 229
Val Lys Lys Leu Cys Gln Ala Thr Phe Pro Thr Leu Leu Cys Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 230
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 230
Val Lys Lys Leu Leu Ala Arg Ser Tyr Leu Tyr Phe Ser Leu Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 231
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 231
Val Lys Lys Leu Leu Tyr Gln Ser Ser Phe Leu Pro Leu Phe Trp Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 232
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 232
Val Lys Lys Leu Leu Ser Ala Ser Phe Leu Ala Phe Arg Ile Thr Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 233
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 233
Val Lys Lys Leu Leu Ser Val Leu Phe Leu Ser His Tyr His Ser Ala
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 234
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 234
Val Lys Lys Leu Leu Pro Leu Ala Leu Leu Tyr Val Arg Leu Ser Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 235
Val Lys Lys Leu Leu Pro Glu Phe Leu Leu Leu Phe Arg Phe Phe Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 236
Val Lys Lys Leu Leu Phe Pro Ser Leu Tyr Ala Trp Gly Gly Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
           2.0
<210> SEQ ID NO 237
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 237
Val Lys Lys Leu Leu Gln Ala Ala Ala Phe Phe Cys Trp Leu Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 238
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 238
Val Lys Lys Leu Leu Pro Phe Phe Leu Phe Cys Ser Ser Leu Arg Ala
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Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 239
<211> LENGTH: 28
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 239
Val Lys Lys Leu Leu Glu Leu Thr Gln Leu Trp Leu Phe His Leu Ala
                        10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 240
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 240
Val Lys Lys Leu Leu Pro Gly Val Pro Leu Leu Cys Phe Arg Ala
                          10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 241
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 241
Val Lys Lys Leu Leu Ser Gln Ala Tyr Leu Ser Tyr Phe Leu Tyr Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 242
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 242
Val Lys Lys Leu Leu Ile Ser Tyr Ala Phe Leu Val Arg Val Thr Ala
Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 243
Val Lys Lys Leu Leu Ala Pro Ala Leu Leu Arg Ser Ile Leu Ala Ala
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                               10
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 244
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<211> LENGTH: 28

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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 244
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Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 245
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 245
Val Lys Lys Leu Leu Ala Val Ser Ala Phe Val Ser Leu Val Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
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<210> SEQ ID NO 246
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 246
Val Lys Lys Leu Leu Thr Leu Ile Thr Phe Lys Phe Leu Pro His Ala
1
                                   10
Ala Gln Pro Ala Met Ala His His His His His
          20
<210> SEQ ID NO 247
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 247
Val Lys Lys Leu Leu Gln Gln Phe Ala Ile Pro Leu Val Glu Phe Ala
1
                                   10
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 248
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 248
Val Lys Lys Leu Leu Met Pro Cys Leu Leu Val Tyr Tyr Leu Glu Ala
Ala Gln Pro Ala Met Ala His His His His His
           20
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 249
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Ala Gln Pro Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 250
Val Lys Lys Leu Leu Ser Leu Ala Leu Leu Arg Val Ser Leu Gly Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 251
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 251
Val Lys Lys Leu Leu Ile Ile Gly Arg Ile Ala Leu Ile Leu Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 252
Val Lys Lys Leu Leu Pro Gln Leu Ile Cys Ala Phe Ile Leu Arg Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 253
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 253
Val Lys Lys Leu Leu Met Val Pro Leu Phe Pro Leu Pro Leu Pro Ala
Ala Gln Pro Ala Met Ala His His His His His
           20
                               25
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 254
Val Lys Lys Leu Leu His Gln Ala Ile Leu Tyr Tyr Tyr Leu Asn Ala
Ala Gln Pro Ala Met Ala His His His His His
<210> SEQ ID NO 255
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 255
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Pro Ala Gln Ala Met
                                  10
Pro Met Ser Arg Met Ala His His His His His
           20
<210> SEO ID NO 256
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 256
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Phe Val Leu Val Arg
                                   10
Glu Ser Ser Met Ala His His His His His
           2.0
<210> SEQ ID NO 257
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 257
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Leu Val Val Ser Ser
Arg Thr Arg Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 258
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ser Arg Pro Arg
                       10
Ala Val Pro Asp Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 259
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Cys Val Ser Val Arg Ser
1
Pro Ala Phe Ala Met Ala His His His His His
<210> SEQ ID NO 260
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 260
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Met Thr Thr Leu Ala Ser
                                  10
Arg Thr His Ala Met Ala His His His His His
          20
                              25
<210> SEQ ID NO 261
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 261
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Leu Ser Met Thr Arg
1 5
                              10
Ser Gly Ala Ala Met Ala His His His His His
          20
<210> SEQ ID NO 262
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 262
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Trp Leu Arg Ser Ser Val
Pro Val Asp Ser Met Ala His His His His His
<210> SEQ ID NO 263
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 263
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ser Ser Leu Thr Arg
                                  10
Asp Ser Ser Ser Met Ala His His His His His
         20
                     25
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 264
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Gly Leu Phe Thr Ile Arg
Asp Ser Phe Ala Met Ala His His His His His
<210> SEQ ID NO 265
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 265
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Trp Leu Gly Ile Thr Lys
Pro Val Trp Ser Met Ala His His His His His
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<210> SEQ ID NO 266
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 266
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Thr Leu Thr Pro Arg
Pro Val Phe Ser Met Ala His His His His His
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<210> SEQ ID NO 267
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 267
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Gln Leu Ala Leu Ser Arg
Pro Ser Phe Pro Met Ala His His His His His
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<210> SEQ ID NO 268
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 268
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Ser Phe Leu Val Ala
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Asp Gln Ser Ser Met Ala His His His His His

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<210> SEQ ID NO 269
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 269
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Gly Leu Ala Ser
Pro Arg Ser Arg Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 270
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Thr Leu Ser Asn Arg
Ser Ala Trp Ser Met Ala His His His His His
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<210> SEQ ID NO 271
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 271
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ser Leu Tyr Pro Thr
             5
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Arg Ser Thr Ala Met Ala His His His His His
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<210> SEQ ID NO 272
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 272
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Thr Thr Leu Ser Arg
Pro Ser Phe Ser Met Ala His His His His His
<210> SEQ ID NO 273
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 273
\label{thm:conditional} \mbox{Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Phe Ser Arg Pro Pro}
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Gln Pro Ser Ser Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 274
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Thr Met Ser Ser Pro Pro
Arg Ser Thr Ser Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 275
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Phe Leu Arg Ile Ser
Pro Ser Ala Ser Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 276
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Phe Leu Arg Pro Ser
Ala Ala Arg Pro Met Ala His His His His His
<210> SEQ ID NO 277
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 277
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Trp Ser Ser Ser Arg
Pro Thr Ser Gln Met Ala His His His His His
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<210> SEQ ID NO 278
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 278
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Leu Val Cys Ser Arg
1 5
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Pro Leu His Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 279
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Leu Gln Arg Pro Pro
Ser Pro Asn Thr Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 280
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ala Met Ala Ser Phe Arg
Pro Arg Asp Gln Met Ala His His His His His
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<210> SEQ ID NO 281
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 281
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Arg Ser Leu Ala Met
Gln Pro Leu Pro Met Ala His His His His His
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<210> SEQ ID NO 282
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 282
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ser Ser Leu Arg Ser
Ser Asn Pro Glu Met Ala His His His His His
           2.0
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<210> SEQ ID NO 283
<211 > LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 283
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Ile Leu Ile Asn Phe
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Arg Ala Ser Ser Met Ala His His His His His
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<210> SEQ ID NO 284
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 284
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Trp Arg Ser Phe Trp
Glu Pro Pro Ala Met Ala His His His His His
<210> SEQ ID NO 285
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 285
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Leu Ala Ala Pro Arg
1
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Ser Thr Val Ala Met Ala His His His His His
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<210> SEQ ID NO 286
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 286
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Gln Tyr Ser Ala Phe Ser
1
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Met Ser Pro Arg Met Ala His His His His His
<210> SEQ ID NO 287
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 287
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Leu Val Ser Ser Lys
Asn Ser Tyr Pro Met Ala His His His His His
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<210> SEQ ID NO 288
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 288
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Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Gly Leu Ser Val Ser Phe
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Arg Thr Ser Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 289
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ala Met Leu Glu Pro Thr
Arg Ser Ser Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 290
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Leu His Arg
Pro Ala Leu Ala Met Ala His His His His His
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<210> SEQ ID NO 291
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 291
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ser Ala Ser Ala Arg
Gly Ser Tyr Ala Met Ala His His His His His
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<210> SEQ ID NO 292
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 292
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Leu Ala Val Thr His
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Arg Ala Tyr Ser Met Ala His His His His His
<210> SEQ ID NO 293
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 293
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Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Phe Ser Leu Ser Arg
Tyr Ser Leu Ala Met Ala His His His His His
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<210> SEQ ID NO 294
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 294
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Leu Ser Ala Pro Arg
His Ala Ser Pro Met Ala His His His His His
<210> SEQ ID NO 295
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 295
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Trp Ser Phe Ser Arg Leu
                                    10
Pro Ser Ser Asp Met Ala His His His His His
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<210> SEQ ID NO 296
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 296
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Leu Ser Leu Thr Lys
Pro Ser Leu Ser Met Ala His His His His His
<210> SEQ ID NO 297
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 297
\label{thm:conditional} \mbox{Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Ser Pro Ala Thr \mbox{Glu}
                                    10
Val Leu Ser Pro Met Ala His His His His His
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<210> SEQ ID NO 298
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Thr Leu Phe Leu Gln Arg
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1
                                   10
Ser Ser Leu Ala Met Ala His His His His His
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<210> SEQ ID NO 299
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 299
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Phe Thr Arg Val Pro
His Lys Pro Ser Met Ala His His His His His
<210> SEQ ID NO 300
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 300
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ala Ile Thr Arg Ser Ser
Gln Phe Pro Ser Met Ala His His His His His
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<210> SEQ ID NO 301
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 301
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Gly Asp Leu Arg Ser
Ser Pro Asp Ala Met Ala His His His His His
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<210> SEQ ID NO 302
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 302
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Thr Thr Leu Ser Thr
              5
                                   10
Arg Cys Tyr Ala Met Ala His His His His His
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<210> SEQ ID NO 303
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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Gly Pro Ala Met Met Ala His His His His His
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<210> SEQ ID NO 304
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 304
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Phe Ser Ser Pro Ser
Ser Arg Ala Pro Met Ala His His His His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 305
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Trp Phe Ser Phe Pro Phe
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Arg Ser Ala Ala Met Ala His His His His His
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<210> SEQ ID NO 306
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 306
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Leu Ser Met Ser Ser
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Pro Ala Arg Ser Met Ala His His His His His
<210> SEQ ID NO 307
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 307
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Trp Ser Leu Cys Arg
Pro Val Cys Ala Met Ala His His His His His
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                               25
<210> SEQ ID NO 308
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 308
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His Ser Trp Ser Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 309
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ile Phe Tyr Thr Thr Arg
Ser Ser Leu Ser Met Ala His His His His His
<210> SEQ ID NO 310
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 310
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ile Tyr Thr Leu Arg Ser
His Ser Met Thr Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 311
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Pro Val Pro Ser Leu Leu
Gly Ser Ala Asp Met Ala His His His His His
<210> SEQ ID NO 312
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 312
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Leu Ser Leu Asn Ser
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Arg Ser Tyr Pro Met Ala His His His His His
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<210> SEQ ID NO 313
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 313
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Ser Pro Thr Ser Gln
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Glu Ile Arg His Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 314
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Phe Ser Cys Pro Leu
Arg Val Ala Ser Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 315
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Leu Ser Leu Asn Arg
                                   10
Gly Val Phe Ala Met Ala His His His His His
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<210> SEQ ID NO 316
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 316
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Pro Gln Val Leu Ser
Ser Ser Pro Gly Met Ala His His His His His
<210> SEQ ID NO 317
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 317
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Val Asn Ala Met Ser
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Ser Pro Arg Pro Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 318
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Ser Ser Trp Cys Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 319
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Asp Leu Ser Ser Asp
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Ser Val Ser Pro Met Ala His His His His His
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<210> SEQ ID NO 320
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 320
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Ile Leu Phe Trp Arg
Asn Thr His Ala Met Ala His His His His His
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<210> SEQ ID NO 321
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 321
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Cys Phe Leu Ser Arg
Ser Ala Phe Ser Met Ala His His His His His
<210> SEQ ID NO 322
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 322
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Phe Met Ile Thr Ser
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                                 10
Lys Ser Arg Ser Met Ala His His His His His
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<210> SEQ ID NO 323
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<211> LENGTH: 28

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<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 323
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ile Val Ser Ser Arg
Gly Ser Phe Ala Met Ala His His His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 324
Ser Pro Ala Ala Met Ala His His His His His
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<210> SEQ ID NO 325
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 325
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Trp Leu Phe Ser Pro Leu
1
                                 10
Arg Ser Tyr Ser Met Ala His His His His His
         20
<210> SEQ ID NO 326
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 326
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Leu Ser Tyr Val Arg
1
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Pro Leu Ser Ala Met Ala His His His His His
<210> SEQ ID NO 327
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 327
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Ile Phe Thr Pro Arg
Ser Val His Ser Met Ala His His His His His
           20
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 328
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Ser Ser Ile Tyr Lys
Asn Ser Pro Pro Met Ala His His His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 329
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Met Ser Asp Ser Thr Ala
Pro Ser Phe Ala Met Ala His His His His His
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<210> SEQ ID NO 330
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 330
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Thr Leu Pro Gln Pro Arg
Phe Pro Ser Pro Met Ala His His His His His
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<210> SEQ ID NO 331
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 331
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Leu Leu Ala Asp Ser
Pro Arg Arg Pro Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 332
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Thr Asp Asn Ser Gly
Glu Pro Ser Leu Met Ala His His His His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 333
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Cys Met Pro Met Ser
Arg Thr Cys Ala Met Ala His His His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 334
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Met Ser Arg Leu Ser Tyr
                                  10
His Thr Pro Ser Met Ala His His His His His
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<210> SEQ ID NO 335
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 335
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ser Asn Ser Arg Val
                                   10
Pro Pro Ser Ser Met Ala His His His His His
          20
<210> SEQ ID NO 336
<211> LENGTH: 28
<212> TYPE: PRT
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<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 336
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Phe Ala Ser Met Arg
His Thr Gln Ala Met Ala His His His His His
<210> SEQ ID NO 337
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 337
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Leu Ser Thr Ile Lys
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Thr Ser Phe Ser Met Ala His His His His His
           20
                               25
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<210> SEQ ID NO 338
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 338
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Gln Gln Ser Ser Leu
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Ser Ser Val Pro Met Ala His His His His His
<210> SEQ ID NO 339
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 339
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Thr Leu Ile Leu Ser His
                                  10
Arg Ser Ser Ala Met Ala His His His His His
          20
                              25
<210> SEQ ID NO 340
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 340
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Phe Ser Arg Asp Pro
1 5
                                10
Ser Phe Thr Ser Met Ala His His His His His
          20
                              25
<210> SEQ ID NO 341
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 341
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ala Leu Ser Pro Thr Arg
His Thr Leu Ala Met Ala His His His His His
<210> SEQ ID NO 342
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 342
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Asn Ile Leu Phe Thr Val
                                  10
Arg Val Tyr Ala Met Ala His His His His His
          20
                      25
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<210> SEQ ID NO 343
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 343
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ala Ser Leu Ser Ala
Arg Cys His Gly Met Ala His His His His His
<210> SEQ ID NO 344
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 344
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Val Thr Leu Ser Leu
                                   10
Arg Ala Ser Ala Met Ala His His His His His
           20
<210> SEQ ID NO 345
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 345
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser His Asp Pro Leu Leu
Leu Ser Ser Pro Met Ala His His His His His
          20
<210> SEQ ID NO 346
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 346
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Trp Ser Leu Ser Ser
Arg Gly Met Thr Met Ala His His His His His
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<210> SEQ ID NO 347
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 347
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ile Ser Tyr Cys Arg
      5
                                   10
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Pro Val Ser Ser Met Ala His His His His His

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20
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<210> SEQ ID NO 348
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 348
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu His Ser Val Glu Leu Pro
Ala Ser Pro Ala Met Ala His His His His His
<210> SEQ ID NO 349
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 349
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ser Thr Ser Arg
Ser Ser Ser Gly Met Ala His His His His His
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<210> SEQ ID NO 350
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 350
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Trp Phe Ser Cys Ser Arg
                                   10
Phe Ala Leu Ser Met Ala His His His His His
          20
<210> SEQ ID NO 351
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 351
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Cys Thr Leu Ser Ser
Arg Ala Phe Ser Met Ala His His His His His
<210> SEQ ID NO 352
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 352
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Ser Pro Leu Ala Arg
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Asn Pro Phe Ser Met Ala His His His His His
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<210> SEQ ID NO 353
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 353
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Phe Ala Phe Ser Arg
Gln Ser Ser Gly Met Ala His His His His His
<210> SEQ ID NO 354
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 354
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Thr Phe Ser Ile Phe Ser
Arg Ala Leu Ala Met Ala His His His His His
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<210> SEQ ID NO 355
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 355
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Leu Phe Phe Ser Ala
Arg Ala Ile Ala Met Ala His His His His His
<210> SEQ ID NO 356
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 356
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Gln Pro Ser Leu Cys
Asp Pro Val Pro Met Ala His His His His His
          20
<210> SEQ ID NO 357
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 357
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ala Ser Tyr His Arg
1 5
                        10
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Val Ala Phe Ala Met Ala His His His His His
           20
<210> SEQ ID NO 358
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 358
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Trp Gln Leu Trp Gln Leu
Pro Ser Arg Pro Met Ala His His His His His
<210> SEQ ID NO 359
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 359
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Thr Pro Met Tyr Arg
                                   10
Pro Thr Ser Pro Met Ala His His His His His
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                               2.5
<210> SEQ ID NO 360
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 360
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Leu Ser Leu His Arg
Phe Ser Phe Ala Met Ala His His His His His
           20
<210> SEQ ID NO 361
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 361
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Tyr Ser His Pro Gln
Asn Ala Leu Ala Met Ala His His His His His
           2.0
                               25
<210> SEQ ID NO 362
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 362
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Val Leu Arg Ser Asp
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Ala Ser Trp Gly Met Ala His His His His His
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<210> SEQ ID NO 363
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 363
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Ser Gly Pro Pro Phe
Asp Arg Thr Ser Met Ala His His His His His
<210> SEQ ID NO 364
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 364
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Cys Ala Leu Ser Arg
1
                                   10
Phe Thr His Ala Met Ala His His His His His
          20
<210> SEQ ID NO 365
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 365
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Phe Ser Leu Ser Arg Pro
1
                                   10
Val Pro Pro Leu Met Ala His His His His His
<210> SEQ ID NO 366
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 366
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Met Asp Ser Phe Ser
Arg Pro Phe Phe Met Ala His His His His His
           20
                               25
<210> SEQ ID NO 367
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 367
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Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Thr Ile Ile Pro Ser
Arg Ala Ser Ser Met Ala His His His His His
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<210> SEQ ID NO 368
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 368
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Pro Ser Ala Asn Pro
Pro Pro Leu Ser Met Ala His His His His His
<210> SEQ ID NO 369
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 369
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Leu Ile Lys Pro Pro
Glu Gly Phe Ser Met Ala His His His His His
           2.0
<210> SEQ ID NO 370
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 370
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ile Ser Thr Leu His Phe
Arg Ala Phe Gly Met Ala His His His His His
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<210> SEQ ID NO 371
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 371
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Arg Val Met Cys Gly
                                   10
His Ser Tyr Ala Met Ala His His His His His
<210> SEQ ID NO 372
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 372
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Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Leu Ser Leu Ser Arg
Thr Phe Ser Gly Met Ala His His His His His
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<210> SEQ ID NO 373
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 373
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Trp Cys Ala Leu Ser Arg
Gln Ser Met Pro Met Ala His His His His His
<210> SEQ ID NO 374
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 374
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Phe Trp Ser Leu Arg
                                   10
Val Ser Trp Pro Met Ala His His His His His
           20
<210> SEQ ID NO 375
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 375
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Ile Leu Ser Pro Arg
Leu Pro Pro Pro Met Ala His His His His His
<210> SEQ ID NO 376
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 376
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Ala Ala His Arg
Phe Ser Tyr Ala Met Ala His His His His His
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<210> SEQ ID NO 377
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
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<400> SEQUENCE: 377
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Val His Leu Thr Ser
1
                                   10
Lys Ala Ile Pro Met Ala His His His His His
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<210> SEQ ID NO 378
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 378
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Ser Leu Thr Leu Tyr Arg
Ser Gly Trp Ser Met Ala His His His His His
<210> SEQ ID NO 379
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 379
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Tyr Tyr Ala Leu Ser Gly
Arg Pro Val Thr Met Ala His His His His His
           20
                               25
<210> SEQ ID NO 380
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 380
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Met Leu Ser Leu Met Arg
Gln Ser Ala Pro Met Ala His His His His His
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<210> SEQ ID NO 381
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 381
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
              5
                                   10
Arg Pro Leu Thr Arg Ile Gln Thr Pro His His
           2.0
<210> SEQ ID NO 382
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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<400> SEQUENCE: 382
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
                                  10
Thr Gln Leu Ser Arg Arg Glu Pro Ser His His
          20
<210> SEQ ID NO 383
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 383
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Ser Leu Ala Thr Ser Pro Ser Arg His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 384
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
Ala Arg Ser Tyr Met Leu Val Arg Pro His His
<210> SEQ ID NO 385
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 385
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
1 5
Arg Ser Tyr Met Leu Leu Ser Arg Pro His His His
<210> SEQ ID NO 386
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 386
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Arg Ser Ala Leu Ala Phe Phe Leu Pro His His
           20
                               25
<210> SEQ ID NO 387
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 387
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Gly Phe Thr Leu Pro Arg Leu Ile His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 388
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Ser Ala Phe Thr Arg Pro Ile Arg Pro His His His
<210> SEQ ID NO 389
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 389
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Arg Tyr Ser His Ala Phe Met Leu Ile His His His
           20
<210> SEQ ID NO 390
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 390
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Pro Met Ser Met Phe Arg Ser Asp His His His
<210> SEQ ID NO 391
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 391
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
                       10
Ser Ser Met Ser Gln Tyr Arg Gln Asn His His
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<210> SEQ ID NO 392
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 392
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Ser Tyr Ser Arg Pro Pro Ser Ile His His
<210> SEQ ID NO 393
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 393
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Ser Ser Met Ser Arg Leu Arg Pro His His His
<210> SEQ ID NO 394
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 394
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
Arg Ser Leu Ser Arg Pro Met Leu Val His His His
           2.0
<210> SEQ ID NO 395
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 395
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Ser Met Ser Leu His Pro Thr Ala His His His
<210> SEQ ID NO 396
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 396
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
                                   1.0
Arg Ser Met Thr Arg Leu Ala Pro Pro His His His
          20
<210> SEQ ID NO 397
<211> LENGTH: 28
<212> TYPE: PRT
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<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 397
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
                                  10
Arg Ala Met Ser Val Ser His Lys Thr His His His
      20
<210> SEQ ID NO 398
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 398
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
                      10
Leu Ala Pro Lys Pro Ser Val Lys Arg His His His
          20
<210> SEQ ID NO 399
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 399
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Pro Ala Pro Ala Leu Ser Arg Leu His His His
           20
<210> SEQ ID NO 400
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 400
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Lys Ala Met Ser Ala Arg Tyr Gln Ser His His His
<210> SEQ ID NO 401
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 401
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Phe
       5
                                 10
Ala Ser Gln Arg Ser Ser Pro Ile Arg His His His
          20
                              25
<210> SEQ ID NO 402
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<211> LENGTH: 28

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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 402
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
Leu Ser Phe Thr Ser Ala Arg Phe Gln His His
<210> SEQ ID NO 403
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 403
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
Ser Ala Ser Ser Arg Leu Ser Pro Lys His His
           20
<210> SEQ ID NO 404
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 404
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
1
                                   10
Arg Ser Tyr Thr Arg Val Pro Leu Ala His His His
          20
<210> SEQ ID NO 405
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 405
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Ser Leu Thr Phe Leu Pro Pro Arg His His His
<210> SEQ ID NO 406
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 406
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Thr Arg Val Asn Ala Phe Met Leu Val His His His
            20
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 407
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gln
Ala Phe Arg Pro Val Pro Val Arg Asn His His
<210> SEQ ID NO 408
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 408
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Ser Gly Met Ser Arg Leu Arg Ser Trp His His His
<210> SEQ ID NO 409
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 409
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Ser Pro Ser Gln Leu Ser Ser Arg His His His
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<210> SEQ ID NO 410
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 410
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Phe Ser Leu Ser Arg Thr Ser Ser Lys His His
<210> SEQ ID NO 411
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 411
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Phe
His Arg Val Gln Gln Phe Ser Pro Ala His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 412
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
Asp Ser Met Leu Thr Phe Arg Arg Ser His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 413
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
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Arg Ser Leu Thr Ser Pro Leu Arg Met His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 414
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Arg Ser Ala Ser Phe Leu Arg Pro Ile His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 415
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Met
Thr Phe Gln Ser Asn Ser Pro Arg Gly His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
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Arg Pro Met Thr Leu Arg Gln Pro Val His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 417
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Val
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Arg Pro Met Ser Arg Val Ile Met Ser His His
<210> SEQ ID NO 418
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 418
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Tyr Gly Phe Ser Arg Pro Phe Ser Lys His His His
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<210> SEQ ID NO 419
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 419
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
1 5
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Arg Ser Cys Phe Ala Phe Met Leu Pro His His
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<210> SEQ ID NO 420
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 420
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Phe Ser Gly Ala Phe Arg Gln Ser Gln His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 421
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
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Arg Ala Gly Ser Phe Ser Ala Ala Pro His His
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<210> SEQ ID NO 422
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 422
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
His Ser Met Ala Pro Pro Ser Arg Arg His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 423
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
Arg Ser Gly Thr Phe Gly Asn Ile Gly His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 424
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Arg Ser Met Ala Ser Thr Pro Leu Ala His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 425
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Val
Tyr Pro Leu Ala Pro Arg Leu Arg Asp His His His
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<210> SEQ ID NO 426
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 426
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Leu Pro Trp Arg Arg Thr Pro Phe Gln His His His
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<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 427
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Met
Arg Thr Pro Pro Leu Ser Gln Arg Ile His His His
<210> SEQ ID NO 428
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 428
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Ser Leu Ser Ser Tyr Asn Ala Val His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 429
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Val
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His Ala Leu Ala Arg Lys Ser Gln Phe His His His
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<210> SEQ ID NO 430
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 430
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Ser Phe Ser Ser Pro Ser Ile Thr His His His
<210> SEQ ID NO 431
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 431
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
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Arg Ala Leu Ser Lys Pro Leu Pro Pro His His His
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<210> SEQ ID NO 432
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<212> TYPE: PRT
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<220> FEATURE:
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<400> SEQUENCE: 432
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
Arg Pro Ser Ala Pro Lys Met Leu Leu His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 433
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Ser Met Ser Tyr Phe Gln Pro Leu His His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 434
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Arg Ser Leu Ser Arg Ser Ile Pro His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 435
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Gln Leu His Gln Ser Pro Gly Asn Pro His His
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<210> SEQ ID NO 436
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 436
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
1 5
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Arg Ala Ile Ala Arg Pro Pro Tyr Thr His His His
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<210> SEQ ID NO 437
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 437
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Ser Leu Ser Thr Val Arg Phe Pro His His His
<210> SEQ ID NO 438
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 438
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Arg Ala Phe Ser Ser Pro Leu Ser Asn His His
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<210> SEQ ID NO 439
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 439
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Asn
Arg Thr Pro Thr Ile Gln Arg Asp Ser His His
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<210> SEQ ID NO 440
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 440
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Ala Val Ser Arg Thr Val Pro Thr His His His
            2.0
<210> SEQ ID NO 441
<211 > LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 441
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
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Gln Ser Met Ala Val Pro Ile Ser Thr His His His
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<210> SEQ ID NO 442
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 442
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
Gln Pro Ser Arg Gly Phe Met Leu Ile His His His
<210> SEQ ID NO 443
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 443
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Arg Ser Met Val Phe Pro Ala Lys Val His His His
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<210> SEQ ID NO 444
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 444
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
1
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Arg Ser Met Thr Leu Lys Gly Pro Glu His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 445
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Phe Pro Phe Ser Arg Gln Pro Asn Ala His His His
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<210> SEQ ID NO 446
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 446
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Arg Ala Leu Thr Ser Ile Ser Gly Met His His
<210> SEQ ID NO 447
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 447
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
Arg Gly Met Ser Leu Asn Val Thr Arg His His
<210> SEQ ID NO 448
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 448
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
His Trp Arg Thr Gln Arg Pro Pro Glu His His
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<210> SEQ ID NO 449
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 449
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Ser Phe Ser Ser Pro Pro Gly Pro His His
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<210> SEQ ID NO 450
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 450
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ile
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Phe Pro Ile Glu Ala Ser Ala Arg Arg His His His
<210> SEQ ID NO 451
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 451
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Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Ser Ser Met Ala Leu Arg Pro Arg Val His His
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<210> SEQ ID NO 452
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 452
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Ala Phe Ser Ser Thr Pro Ala Met His His
<210> SEQ ID NO 453
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 453
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Arg Ser Met Val Leu Gln Gly Pro Thr His His His
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<210> SEQ ID NO 454
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 454
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Ser Met Thr Ser Pro Pro Tyr Ile His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 455
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
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Asn Arg Pro Gln Ser Thr Lys Asn Ile His His
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<210> SEQ ID NO 456
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Arg Ala Leu Thr Met Thr Pro Ser Phe His His His
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<210> SEQ ID NO 457
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 457
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
Thr Arg Leu Phe Ala Phe Met Leu Thr His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 458
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Ala Met Ser Pro Ile Pro Arg Gln His His
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<210> SEQ ID NO 459
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 459
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Ser Met Gly Ser Met Trp Gln Leu His His
<210> SEQ ID NO 460
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 460
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
              5
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Phe Ser Met Thr Arg Ser Ser Pro Leu His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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<400> SEQUENCE: 461
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Phe Ser Phe Thr Arg Gln Pro Leu Pro His His
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<210> SEQ ID NO 462
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 462
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Asn
Arg Val Pro Ser Pro Ala Ser Gln Thr His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 463
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Phe Ser Phe Ser Lys Pro Arg Phe Ser His His
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<210> SEQ ID NO 464
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 464
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
1 5
Arg Ser Leu Thr Gln Phe Ser Ser Val His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 465
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Cys Phe Ser Ser Pro Val Ala Leu His His His
          20
                               25
<210> SEQ ID NO 466
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 466
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gly
Ala Ser Ser Trp Trp Leu Phe Pro Ser His His
<210> SEQ ID NO 467
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 467
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Pro Pro Gln Gln Gln Ala Leu Leu Ser His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 468
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Gly Phe Ser Met Ala Phe Phe Pro His His
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<210> SEQ ID NO 469
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 469
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Leu Ala Met Ser Arg Pro Gln Ala Ser His His
<210> SEQ ID NO 470
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 470
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Tyr Ala Leu Thr Thr Phe Gln Ser Val His His
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<210> SEQ ID NO 471
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 471
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gln
His Ala Phe Thr Arg Pro Phe Arg Val His His
           20
                                25
<210> SEQ ID NO 472
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 472
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Ala Phe Ser Ser Pro Ser Gly Ser His His
<210> SEQ ID NO 473
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 473
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Ser Ala Leu Ala Arg Ser Pro Arg Val His His His
           2.0
<210> SEQ ID NO 474
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 474
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
Arg Ala Met Ser Ser Pro Phe Arg Pro His His His
<210> SEQ ID NO 475
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 475
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Thr Phe Ala Arg Ser Phe Met Leu Thr His His His
<210> SEQ ID NO 476
<211> LENGTH: 28
<212> TYPE: PRT
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<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 476
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Phe
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Pro Leu Ser Ser Arg Ala Phe Met Leu His His
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<210> SEQ ID NO 477
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 477
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
                      10
Arg Ser Met Ser Thr Ser Pro Ile Leu His His His
         20
<210> SEQ ID NO 478
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 478
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Phe Gly Leu Gln Leu Pro Gln Pro Phe His His His
          20
                               25
<210> SEQ ID NO 479
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 479
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Ser Met Ser Leu Ser Ser Asp Leu His His His
<210> SEQ ID NO 480
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 480
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
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Phe Pro Leu Ala Arg Arg Pro Ile Asn His His
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<210> SEQ ID NO 481
<211> LENGTH: 28
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 481
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Ser Cys Arg Ala Met Thr Leu Pro Arg His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 482
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Tyr Pro Phe Ser Arg Ala Gly Pro Pro His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 483
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
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Asn Gln Gln Ala Leu Pro Phe Gln Leu His His
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<210> SEQ ID NO 484
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 484
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gly
Trp Ser Met Ser Leu Arg Ser His Ser His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 485
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Pro Gln Val Val Thr Arg Lys Asp Leu His His
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<212> TYPE: PRT
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<220> FEATURE:
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<400> SEQUENCE: 486
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
Arg Asn Ala His Ala Met Ala Ser Ala His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 487
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Ser Gly Ser Phe Asn Val Thr Pro His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 488
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Pro Leu Ser Arg Val Pro Val Phe His His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 489
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Lys Arg Met Pro Pro Pro Ile Ser Gln His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 490
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Arg Ser Met Ser Ser Leu Pro Ser Pro His His
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<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 491
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
Arg Ser Ser Ser Ile Phe Pro Leu His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 492
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Arg
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Ser Ala His Ala Met Ser Ile Gln Thr His His His
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<210> SEO ID NO 493
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
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Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gly
Tyr Cys Phe Ser Ala Arg Ile Ile Arg His His His
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<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 494
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
His Leu Ser Pro Leu Gln Pro Gln Gln His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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Phe Ser Phe Ser Arg Phe Pro Gly Leu His His
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<212> TYPE: PRT
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<220> FEATURE:
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<400> SEQUENCE: 496
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Ser Ser Met Ser Leu Arg Pro Gln Phe His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 497
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Ser Pro Arg Ala Arg Pro Val Pro Pro His His His
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<210> SEQ ID NO 498
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 498
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
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Arg Ser Leu Ser Ala Leu Ser Pro Tyr His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 499
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
Val Arg Gln Leu His Thr Asn Leu Arg His His His
<210> SEQ ID NO 500
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 500
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
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Thr Thr Ser Thr Pro Tyr Gln Ser Pro His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
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<400> SEQUENCE: 501
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Asn Ala Leu Thr Phe Leu Pro Ser Gln His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 502
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Arg Ser Leu Ser Ser Pro Leu Thr Leu His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<400> SEQUENCE: 503
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Arg Pro Pro Thr Val Gly Leu Arg Gln His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 504
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Arg Ala Leu Ser Pro Met Ser Trp Gln His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 505
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Val
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Phe Pro Phe Ser Arg Pro Leu Leu Arg His His His
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<210> SEQ ID NO 506
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<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 506
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Val
Pro Arg Cys Leu Ser Met Ser Leu Gly His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 507
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gln
Gln Pro Ser Phe His Pro Ile Ser Arg His His
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<210> SEQ ID NO 508
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 508
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Lys Ala Phe Ser Ser Phe Gln Ala Ser His His
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<210> SEQ ID NO 509
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 509
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gly
Tyr Ser Met Ser Gln Ser Gly Leu Thr His His His
<210> SEQ ID NO 510
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 510
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
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Gln Ala Leu Thr Thr Arg Gly Leu Ala His His His
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<210> SEQ ID NO 511
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
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<400> SEQUENCE: 511
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Val
Lys Ser Leu Thr Arg Pro Ala Phe Leu His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 512
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Gln Ser Arg Leu Arg Val Tyr Pro Pro His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 513
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
Ala Ile Gly Phe Met Leu Leu Arg Tyr His His
<210> SEQ ID NO 514
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 514
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Phe Gly Thr Leu Val Arg Pro Arg Pro His His His
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<210> SEQ ID NO 515
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 515
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ile
1 5
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Arg Arg Pro Val Asp Pro Val Met Pro His His His
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<210> SEQ ID NO 516
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 516
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Phe
Pro Leu Arg Gln Thr His Arg Tyr Pro His His His
<210> SEQ ID NO 517
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 517
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
His Ser Met Gln Arg Pro Thr Gly Arg His His
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<210> SEQ ID NO 518
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 518
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Arg
His Thr Gln Leu Ser Ser Ser Thr Ser His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 519
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Cys Gly Phe Ser Arg Leu Ser Lys Ala His His His
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<210> SEQ ID NO 520
<211 > LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 520
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Arg Ser Phe Ser Gln Leu Pro His Ile His His
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<210> SEQ ID NO 521
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 521
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Ser Ser Met Ser Gln Leu Arg Pro Phe His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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Arg Thr Thr Phe Ala Leu Gln Ser Ser His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 523
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
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Gln Ser Met Ser Ile Arg His Asn Asn His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 524
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Asn
Ser Arg Phe Arg Thr Thr Pro Pro Ser His His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 525
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Val Ser Met Ser Arg Tyr Gln Leu Ser His His
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<210> SEQ ID NO 526
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 526
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Ser Gly Ala Ser Arg Leu Arg Ile Leu His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 527
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
Trp Ser Leu Ser Arg Pro Arg Leu Leu His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 528
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Ser Arg Ser Thr Lys Leu Thr Pro Ser His His
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<210> SEQ ID NO 529
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 529
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Arg Val Ser Val Ala Phe Met Leu Met His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 530
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Leu Gly Arg Ser Met Ala Pro Gly Pro His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 531
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Phe
Val His Arg Arg Asp Ser Ser Ser Leu His His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 532
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Leu Gly Phe Ser Arg Leu Thr Ser Leu His His
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<210> SEQ ID NO 533
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 533
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Ser Ala Leu Ser Arg Arg Val Pro Gln His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 534
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Tyr Pro Ala Ser Trp Pro Arg Leu Arg His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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Arg Val Ser Leu Ala Val Thr Pro Ser His His
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<210> SEQ ID NO 536
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 536
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Asn
Asn Pro Phe Ser Ser Leu Ser Gln Gln His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 537
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Arg
Pro Leu Pro Arg Pro Phe Ala Gly Asn His His
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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 538
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gly
Phe Ser Met Thr Gln Tyr Leu Pro Gln His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 539
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Ser Ala Leu Ser Arg Ser Phe Tyr Pro His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
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<400> SEQUENCE: 540
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
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Gln Gln Arg Cys Phe Ala Met His Ile His His
<210> SEQ ID NO 541
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 541
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ile
Lys His Phe Tyr Asn Ser Arg Pro Ser His His His
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 542
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Phe
Thr Arg Leu Pro Lys Glu Ser Ser Pro His His His
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<210> SEQ ID NO 543
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 543
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
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Pro Ala Gln Pro Arg Val Thr Arg Thr His His His
<210> SEQ ID NO 544
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 544
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
Arg Ser Met Thr Leu Asn Thr Ser Thr His His His
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                               25
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 545
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
Asp Thr Phe Ser Tyr Ser Ser Gln Asp His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 546
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Phe
Arg Asn Pro Gln Leu Pro Ser Ser Ala His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 547
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Phe
Arg Pro Asp Arg Thr Pro Pro Ser Ser His His
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<210> SEQ ID NO 548
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<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 548
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gln
Ser His Thr Ile Leu Pro Leu Pro Ala His His His
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<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 549
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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Ser Ala Phe Gln Pro Met Val Ser Ser His His His
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<212> TYPE: PRT
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 550
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gln
Ser Arg Arg Leu Pro Ile Leu Pro Leu His His His
<210> SEQ ID NO 551
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 551
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gly
Gln Ala Tyr Leu Pro Ala Pro Gln Leu His His His
<210> SEQ ID NO 552
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 552
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Ser Arg Pro Arg Glu Thr Leu Phe Leu His His His
<210> SEQ ID NO 553
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 553
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Ala Ala Ser Val Val Arg Ser Arg Asp His His His
<210> SEQ ID NO 554
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 554
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Val
                                    1.0
Arg Gly Ala Ala Pro Lys Phe Ser Val His His His
<210> SEQ ID NO 555
<211> LENGTH: 28
<212> TYPE: PRT
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<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 555
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Phe
                                  10
Arg His Gln Pro Ala Ser Val Ser Thr His His
<210> SEQ ID NO 556
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 556
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
      5
                       10
Thr Asn Ala Ile Ala Phe Phe Leu Gln His His His
          20
                              25
<210> SEQ ID NO 557
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 557
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
Lys Ser Leu Arg Ser Asp Thr Pro Asn His His His
          20
<210> SEQ ID NO 558
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 558
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ile
Lys Arg Pro Leu Pro Leu Ala Pro Thr His His His
<210> SEQ ID NO 559
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 559
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
            5
                                 10
Ser Ser Ser Lys Ser Arg Phe Met Leu His His His
                        25
         20
<210> SEQ ID NO 560
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<211> LENGTH: 28

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<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 560
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
Trp Lys Pro Arg Leu Leu Pro Pro Gln His His His
<210> SEQ ID NO 561
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 561
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Arg Gly Phe Met Leu Thr Leu Arg Tyr His His His
           20
<210> SEQ ID NO 562
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 562
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
1
                                   10
Lys Ala Arg Gly Ile Met Pro Val Phe His His His
          20
<210> SEQ ID NO 563
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 563
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Ser Leu Pro Arg Leu Thr Ser Gln Ser His His
<210> SEQ ID NO 564
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 564
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gln
Ser Ser Ala Phe Ser Tyr Met Leu Ser His His
           20
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<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 565
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Phe Ser Ser Gln Arg Phe Leu Arg Pro His His
<210> SEQ ID NO 566
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 566
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Ser Ser Asn Thr Ser Arg Arg Phe Pro His His His
           20
<210> SEQ ID NO 567
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 567
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Asn
Gln Thr Ala Ala Thr Ala Pro Pro Arg His His His
           20
<210> SEQ ID NO 568
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 568
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gly
Ala Pro Leu Ser Trp Arg Arg Ser Tyr His His
<210> SEQ ID NO 569
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 569
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
Arg Ser Val Trp Cys Ile Pro Arg Pro His His His
            20
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<210> SEQ ID NO 570
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 570
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
Lys Ala Cys Leu Arg Pro Leu Gln Thr His His His
<210> SEQ ID NO 571
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 571
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
                                   10
Leu Ala Ser Ser His Arg His Arg Pro His His
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<210> SEO ID NO 572
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEOUENCE: 572
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
                                   10
Arg Ala Asp Ser Leu Ala Pro Lys Ser His His His
           2.0
<210> SEQ ID NO 573
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 573
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Val Pro Gln Phe Ser Gly Arg Ser Arg His His His
<210> SEQ ID NO 574
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 574
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Val
                                  10
Tyr Pro Ala Arg Phe Pro Ala Lys Thr His His His
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<210> SEQ ID NO 575
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 575
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Asn
1
Phe Met Leu Arg His Pro Gln Thr Phe His His His
<210> SEQ ID NO 576
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 576
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Tyr
                                  10
Val Pro Arg Phe Pro Pro Lys Ser Ala His His His
           20
<210> SEQ ID NO 577
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 577
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
1 5 10
Ser Pro Met Ser Arg Thr Arg Tyr Val His His
          20
                               25
<210> SEQ ID NO 578
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 578
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Tyr Pro Leu Thr Lys Pro Tyr Arg Pro His His His
<210> SEQ ID NO 579
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 579
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
                                  10
Ser Tyr Trp Ser His Arg Lys Pro Pro His His His
          20
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<210> SEQ ID NO 580
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 580
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Pro Arg Thr Phe Ala Phe Phe Leu Met His His His
<210> SEQ ID NO 581
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 581
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Leu
Gly Pro Gly Ile Arg Lys Lys Pro Ala His His His
           20
<210> SEQ ID NO 582
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 582
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
Arg Leu Cys Val Ala Lys Val Ala Gly His His
          20
<210> SEQ ID NO 583
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 583
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Arg
Ser Leu Pro Ala Ser Gly Ala Ser Arg His His His
          20
<210> SEQ ID NO 584
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 584
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ala
             5
Ser Pro Arg Val Lys Ser Tyr Ser Pro His His His
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20
                                25
<210> SEQ ID NO 585
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 585
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
Ser Arg Thr Phe Ala Phe Tyr Leu Val His His His
<210> SEQ ID NO 586
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 586
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Gln
Gln Glu Phe Ala Met Ala His His His His His
           20
<210> SEQ ID NO 587
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 587
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Pro
              5
Gln Ser Ser Lys Ala Phe Phe Leu Asn His His
<210> SEQ ID NO 588
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 588
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Val
Lys Ala Leu Arg Gly Ser Tyr Pro Thr His His His
<210> SEQ ID NO 589
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 589
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Thr
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Gln Pro Ser Gln Val Arg Tyr Met Leu His His His
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<210> SEQ ID NO 590
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 590
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Ala Arg Gly Gln His Val Arg Pro Pro His His His
<210> SEQ ID NO 591
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 591
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
Thr Arg Cys Pro Gly Phe Phe Leu Gln His His
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<210> SEQ ID NO 592
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: artificial
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 592
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Cys
Pro Ser Val Phe Ser Arg Thr Pro Pro His His
<210> SEQ ID NO 593
<211> LENGTH: 28
<212> TYPE: PRT
<213 > ORGANISM: artificial
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic polypeptide
<400> SEQUENCE: 593
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Asp
Ala Ser Ser Trp Arg His Phe Leu Ser His His His
          20
                                25
<210> SEQ ID NO 594
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: the wild-type M13 signal peptide N-terminal
     to gene III
<400> SEQUENCE: 594
Met Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Ser
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5
                                    10
                                                         15
His Ser
<210> SEQ ID NO 595
<211> LENGTH: 22
<212> TYPE: PRT
<213 > ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: the pelB signal sequence of Pectobacterium
      wasabiae
<400> SEQUENCE: 595
Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Ala
Ala Gln Pro Ala Met Ala
<210> SEQ ID NO 596
<211> LENGTH: 30
<212> TYPE: PRT
<213 > ORGANISM: artificial sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Signal peptide
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (6)..(6)
<223 > OTHER INFORMATION: A, C, F, G, I, L, M, P, Q, S, V, W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (7)..(7)
<223> OTHER INFORMATION: A, D, F, G, H, I, L, M, N, P, S, T, V, or W
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (8) .. (8)
<223> OTHER INFORMATION: A, F, G, L, M, P, Q, R, S, T, V, or W
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (9) .. (9)
<223> OTHER INFORMATION: A, F, G, H, I, L, M, P, Q, R, S, T, V, W, or Y
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<221> NAME/KEY: VARIANT
<222> LOCATION: (10) .. (10)
<223> OTHER INFORMATION: A, C, D, F, G, H, I, L, M, P, Q, R, S, T, V, W,
      or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (11) .. (11)
<223> OTHER INFORMATION: A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T,
     V, W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T,
     V, W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (13)..(13)
<223> OTHER INFORMATION: A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S,
     T, V, W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (14)..(14)
<223> OTHER INFORMATION: A, C, D, E, F, G, H, I, L, M, N, P, Q, R, S, T,
     V,W, or Y
<220> FEATURE:
<221 > NAME/KEY: VARIANT
<222> LOCATION: (15) .. (15)
<223> OTHER INFORMATION: A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S,
      T, V,W, or Y
<400> SEQUENCE: 596
Val Lys Lys Leu Leu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Ala
             5
1
                                   10
```

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Ala Gln Pro Ala Met Ala His His His His His Gly His
            2.0
                                25
<210> SEQ ID NO 597
<211> LENGTH: 30
<212> TYPE: PRT
<213 > ORGANISM: artificial sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Signal peptide
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (11)..(11)
<223 > OTHER INFORMATION: A, C, F, G, H, I, L, M, N, P, Q, S, T, V, W, or
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: A, C, D, F, G, H, I, L, M, P, Q, R, S, T, V, W,
     or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (13)..(13)
<223> OTHER INFORMATION: A, C, D, F, G, H, I, L, M, N, P, Q, R, S, T, V,
     W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (14)..(14)
<223 > OTHER INFORMATION: A, C, E, F, H, I, K, L, M, N, P, Q, R, S, T, V,
     W. or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (15)..(15)
<223> OTHER INFORMATION: A, C, D, F, H, I, L, M, N, P, Q, R, S, T, V, W,
     or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (16) .. (16)
<223> OTHER INFORMATION: A, C, D, E, F, G, H, K, L, M, P, Q, R, S, T, V,
     W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (17)..(17)
<223> OTHER INFORMATION: A, D, E, F, G, H, K, L, M, N, P, Q, R, S, T, V,
     or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (18)..(18)
<223> OTHER INFORMATION: A, C, F, G, I, K, L, M, N, P, Q, R, S, T, or V
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (19)..(19)
<223> OTHER INFORMATION: A, C, D, F, H, I, L, M, N, P, Q, R, S, T, V, W,
     or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (20)..(20)
<223> OTHER INFORMATION: A, C, D, E, F, G, H, L, M, P, Q, R, S, or T
<400> SEQUENCE: 597
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Xaa Xaa Xaa Xaa Xaa Xaa
Xaa Xaa Xaa Met Ala His His His His His Gly His
            2.0
                                25
<210> SEQ ID NO 598
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Signal peptide
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (16)..(16)
<223> OTHER INFORMATION: A, C, D, F, G, I, L, M, N, P, Q, R, S, T, V, or
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<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (17)..(17)
<223> OTHER INFORMATION: A, C, D, F, G, H, K, L, N, P, Q, R, S, T, V, W,
     or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (18)..(18)
<223> OTHER INFORMATION: A, C, E, F, G, H, I, K, L, M, N, P, Q, R, S, T,
      V, W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (19)..(19)
<223 > OTHER INFORMATION: A, C, D, F, G, H, I, L, M, N, P, Q, R, S, T, V,
      W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (20)..(20)
<223> OTHER INFORMATION: A, C, E, F, G, H, I, K, L, M, N, P, Q, R, S, T,
    W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (21)..(21)
<223 > OTHER INFORMATION: A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S,
     T, V, W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (22)..(22)
<223> OTHER INFORMATION: A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T,
     V. or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (23)..(23)
<223> OTHER INFORMATION: A, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V,
     W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (24)..(24)
<223> OTHER INFORMATION: A, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V,
     W, or Y
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (25)..(25)
<223> OTHER INFORMATION: A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T,
     V, or Y
<400> SEOUENCE: 598
Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr Xaa
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa His His Gly His
            20
                                25
<210> SEQ ID NO 599
<211> LENGTH: 4
<212> TYPE: PRT
<213 > ORGANISM: Artificial sequence
<220> FEATURE:
<223 > OTHER INFORMATION: Synthetic peptide
<400> SEQUENCE: 599
Ile Glu Gly Arg
1
<210> SEQ ID NO 600
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                                                                         48
                                    10
aac gtg aaa aaa tta tta ttc gca att cct tta gtt gtt cct ttc tat
                                                                         96
Asn Val Lys Lys Leu Leu Phe Ala Ile Pro Leu Val Val Pro Phe Tyr
            2.0
                                 25
geg gee cag eeg gee atg gee cat cat cae cae cat cat gge cae ggg
                                                                        144
Ala Ala Gln Pro Ala Met Ala His His His His His Gly His Gly
        35
                            40
tcc ggc gat att caa atg
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Ser Gly Asp Ile Gln Met
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                                    10
cac cat cat ggc cac ggg tcc ggc gat att caa atg acc cag agc ccg
His His Gly His Gly Ser Gly Asp Ile Gln Met Thr Gln Ser Pro
age age etg age geg age gtg gga gat ege gtg ace att ace tge egt
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
                                                                          144
gcg agc cag gat gtt agc acg gcg gtc gca tgg tat cag cag aaa cca Ala Ser Gln Asp Val Ser Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro
                                                                          192
ggc aaa gcg ccg aaa ctt ctg ata tac tct gcg tcc ttc ctg tat agc
                                                                          240
Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser
                     70
                                          75
                                                                          288
ggc gtg ccg tcg cgt ttt tcg ggc agt ggc agc ggc acg gac ttt acc
Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
                 85
                                      90
ctg acg ata tct tcc tta caa ccg gag gat ttt gcg acc tac tac tgt
Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
            100
                                  105
                                                       110
caa cag cat tat acc aca ccg ccg acc ttc ggt tgt ggc acc aaa gtg
                                                                          384
Gln Gln His Tyr Thr Thr Pro Pro Thr Phe Gly Cys Gly Thr Lys Val
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	309		310
		-continued	
115	120	125	
		gag ggc cgt agc gga ggt Glu Gly Arg Ser Gly Gly 140	432
	n Leu Val Glu Ser	gga ggc ggt ctg gtg caa Gly Gly Gly Leu Val Gln 155 160	480
		gcg agc ggg ttc acc att Ala Ser Gly Phe Thr Ile 175	528
		get eec gge aag tgt etg Ala Pro Gly Lys Cys Leu 190	576
		ggt tac aca tat tat gcc Gly Tyr Thr Tyr Tyr Ala 205	624
		gcg gac acc agc aaa aat Ala Asp Thr Ser Lys Asn 220	672
	t Asn Ser Leu Arg	gcg gaa gac aca gcg gtg Ala Glu Asp Thr Ala Val 235 240	720
		ccg tat gcg atg gat tat Pro Tyr Ala Met Asp Tyr 255	768
		tog gog toa gog god goa Ser Ala Ser Ala Ala Ala 270	816
ggt gcg ccg gtg ccg ta Gly Ala Pro Val Pro Ty 275		gaa ccg cgt gcc gca tag Glu Pro Arg Ala Ala 285	864
act gtt gaa agt tgt tt Thr Val Glu Ser Cys Le 290			900
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His His His Gly His Gl 20	y Ser Gly Asp Ile 25	Gln Met Thr Gln Ser Pro 30	
Ser Ser Leu Ser Ala Se 35	r Val Gly Asp Arg 40	Val Thr Ile Thr Cys Arg 45	
Ala Ser Gln Asp Val Se 50	r Thr Ala Val Ala 55	Trp Tyr Gln Gln Lys Pro	
Gly Lys Ala Pro Lys Le 65 70	_	Ala Ser Phe Leu Tyr Ser 75 80	
Gly Val Pro Ser Arg Ph 85	e Ser Gly Ser Gly 90	Ser Gly Thr Asp Phe Thr 95	
Leu Thr Ile Ser Ser Le 100	u Gln Pro Glu Asp 105	Phe Ala Thr Tyr Tyr Cys 110	

Gln Gln His Tyr Thr Thr Pro Pro Thr Phe Gly Cys Gly Thr Lys Val \$115\$ \$120\$ \$125\$

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Glu Ile Lys Arg Gly Gly Gly Ser Ile Glu Gly Arg Ser Gly Gly 130 $135$
Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ile
Ser Asp Tyr Trp Ile His Trp Val Arg Gln Ala Pro Gly Lys Cys Leu
Glu Trp Val Ala Gly Ile Thr Pro Ala Gly Gly Tyr Thr Tyr Tyr Ala
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn 210 215 220
Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
Tyr Tyr Cys Ala Arg Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr
                   250
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Ala Ala Ala
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Thr Val Glu Ser Cys Leu Ala Lys Pro His Thr Glu
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We claim:

- 1. An isolated nucleic acid, comprising
- a first nucleotide sequence encoding a signal peptide, and a second nucleotide sequence encoding a single chain antibody capable of forming an interface disulfide bond, the second nucleotide sequence being located 3' downstream to the first nucleotide, wherein the signal peptide has the amino acid sequence of
- $\begin{array}{l} VKKLLX_{1}X_{2}X_{3}X_{4}X_{5}X_{6}X_{7}X_{8}X_{9}X_{10}AAQPAMA & HHH-\\ HHHGH (SEQ ID NO:596), in which <math>X_{1}$ is $A, C, F, G, I, L, M, P, Q, S, V, W, or Y; <math>X_{2}$ is $A, D, F, G, H, I, L, M, N, P, S, T, V, or W; <math>X_{3}$ is $A, F, G, L, M, P, Q, R, S, T, V, or W; <math>X_{4}$ is $A, F, G, H, I, L, M, P, Q, R, S, T, V, W, or Y; <math>X_{5}$ is $A, C, D, F, G, H, I, L, M, P, Q, R, S, T, V, W, or Y; <math>X_{6}$ is $A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; <math>X_{7}$ is $A, C, D, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; <math>X_{8}$ is $A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; <math>X_{9}$ is $A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y; and <math>X_{10}$ is $A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, or Y. W, or Y. \\ \end{array}$
- 2. The nucleic acid of claim 1, further comprising a third nucleotide encoding a phage coat protein, the third nucleotide sequence being located 3' downstream to the second nucleotide sequence.
- 3. The nucleic acid of claim 1, wherein the nucleic acid is 65 an expression vector for expression a fusion protein containing the signal peptide and the single chain antibody.

- **4**. The nucleic acid of claim **1**, wherein the single chain antibody contains a first variable region, a second variable region, and a protein linker connecting the first and the second variable region, wherein the first and the second variable region are stabilized by an interface disulfide bond.
- 5. The nucleic acid library of claim 4, wherein the first variable region is a heavy chain variable region (V_H) or a light chain variable region (V_L) .
- **6**. The nucleic acid library of claim **4**, wherein the second variable region is a heavy chain variable region (V_H) or a light chain variable region (V_L) .
- 7. The nucleic acid of claim 3, wherein the expression vector is a phagemid.
 - 8. A host cell containing the nucleic acid of claim 4.
- **9**. A phage containing a disulfide-stabilized single chain antibody fused with its coat protein on the surface, wherein the phage is prepared by the method comprising the steps of: providing a host cell of claim **8**, and
 - culturing the host cell in a medium under conditions allowing expression of the phage.
- 10. A method for producing a disulfide-stabilized single chain antibody, comprising
 - providing a host cell containing an expression construct,
 - culturing the host cell in a medium under conditions allowing expression of the disulfide-stabilized single chain antibody,

wherein the expression construct includes a first nucleotide sequence encoding a signal peptide, and a second nucleotide sequence encoding a single chain antibody capable of forming an interface disulfide bond, the second nucleotide sequence being located 3' downstream to the first 5 nucleotide, and

11. The method of claim 10, wherein the single chain 20 antibody contains a first variable region, a second variable region, and a protein linker connecting the first and the second

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variable region, wherein the first and the second variable region are stabilized by an interface disulfide bond.

- 12. The method of claim 11, wherein the first variable region is a heavy chain variable region (V_H) or a light chain variable region (V_L) .
- 13. The method of claim 11, wherein the second variable region is a heavy chain variable region (V_H) or a light chain variable region (V_L) .
- 14. The method of claim 10, further comprising, after the culturing step, collecting the medium for isolating the disulfide-stabilized single chain antibody.
- 15. The method of claim 10, wherein the expression construct is a phagemid that further includes a third nucleotide encoding a phage envelope protein, the third nucleotide sequence being located 3' downstream to the second nucleotide sequence.
- 16. The method of claim 15, further comprising, after the culturing step, collecting the medium for isolating phage particles that display the disulfide-stabilized single chain antibody.

* * * * *